

XII Meeting. State of the Art in

HEART FAILURE

CLINICAL PRACTICE AND ORGANIZATIONAL MODELS

Venue: Hotel Meliá María Pita, A Coruña

A Coruña 26-27 September 2025



#ACORUÑAHF2025



Valvular Interventions in HF. Where are we Going?

Defining “optimal medical management” at pre- and post-intervention. HF Clinician’s view

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Disclosures

Lecture Honoraria, Advisory Board, Travel Support:

Anylam, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Fresenius, Imedos, Medtronic, Mepha, MSD, Mundipharma, Novartis, Orion Pharma, Pierre Fabre, Pfizer, Roche, Schwabe Pharma, Vifor, Zoll

Research Grants:

Bayer, Novartis, AstraZeneca, Berlin Heart

National Coordinator:

Alexion/Astra: DepleTTR-CM study

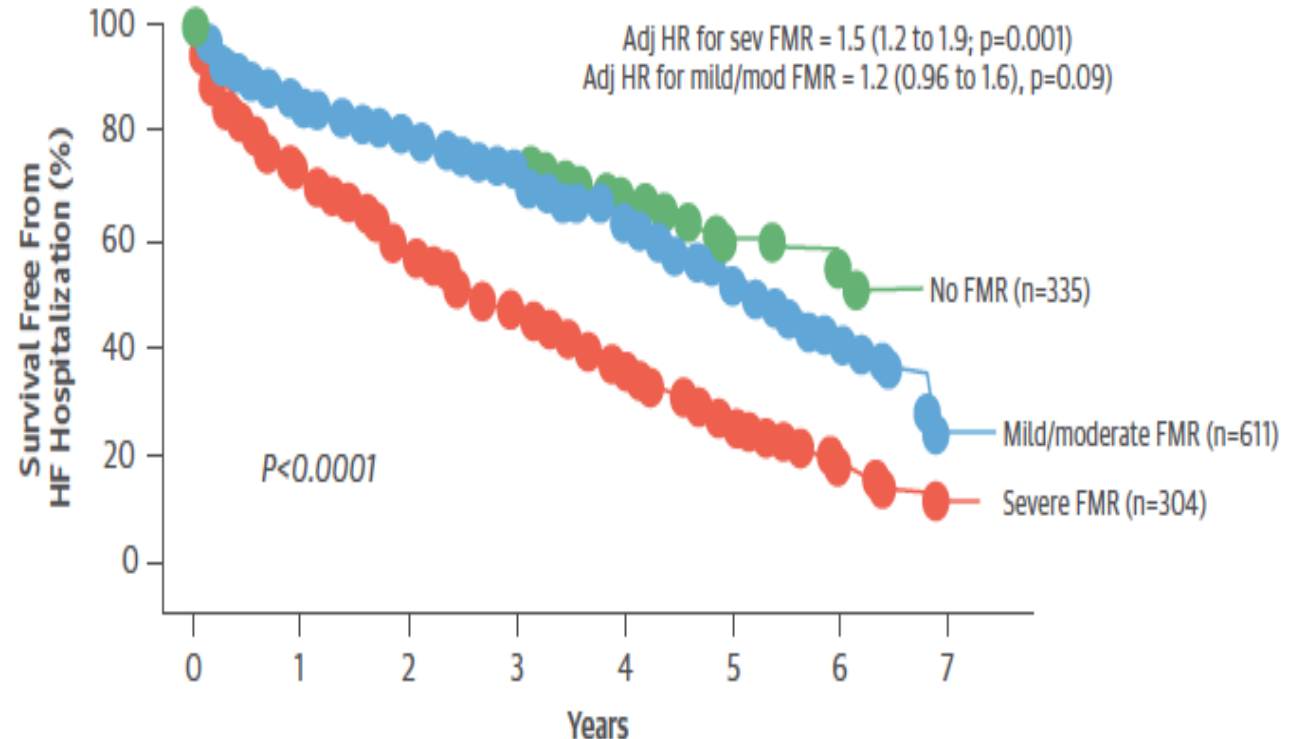
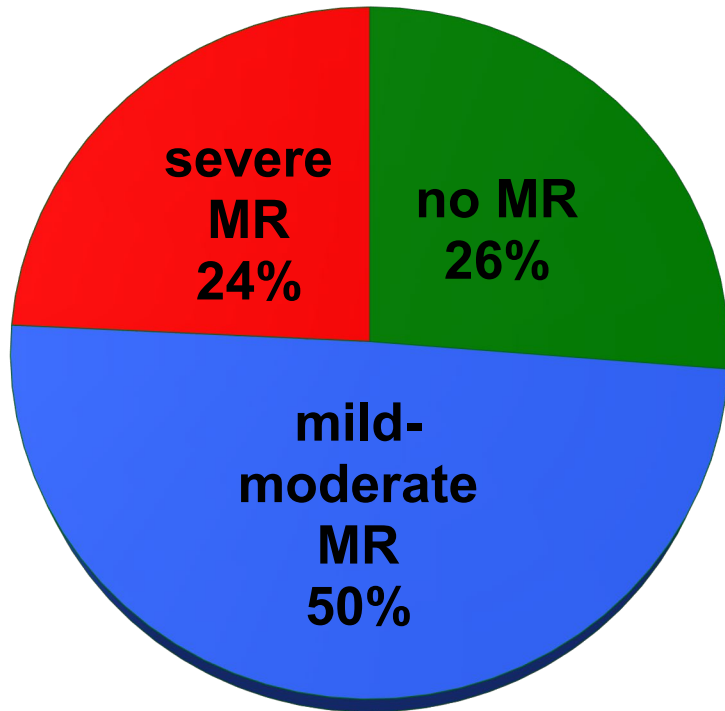
Mitral Regurgitation

3/4 of Patients with Heart Failure present with FMR

Prognosis determined by the underlying disease

1256 pts with ischemic or non-ischemic DCM (mean EF 32%)

Presence of MR is associated with increased mortality



4 columns to improve mortality and morbidity in HFrEF (Class I, A or B)



**ACE-Inhibitor
Sacubitril/Valsartan
(ARB)**

Beta-Blocker

**Mineralocorticoid
Receptor Antagonist**

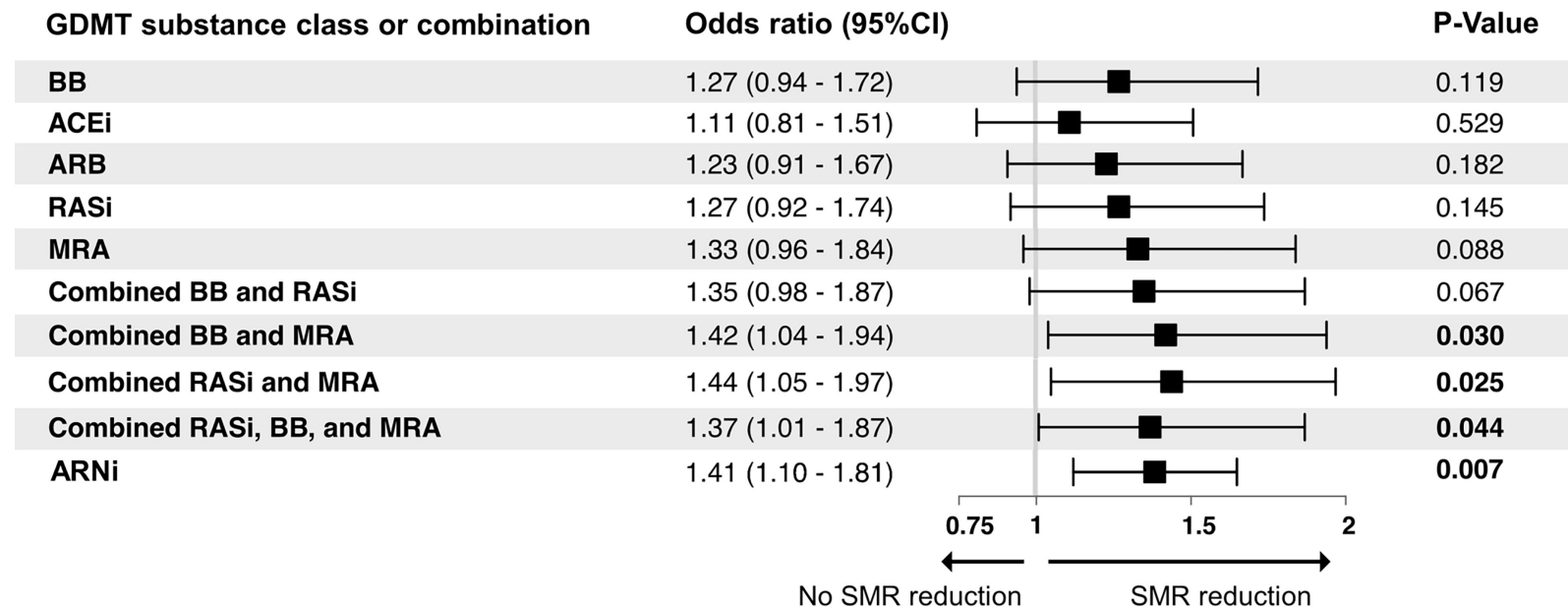
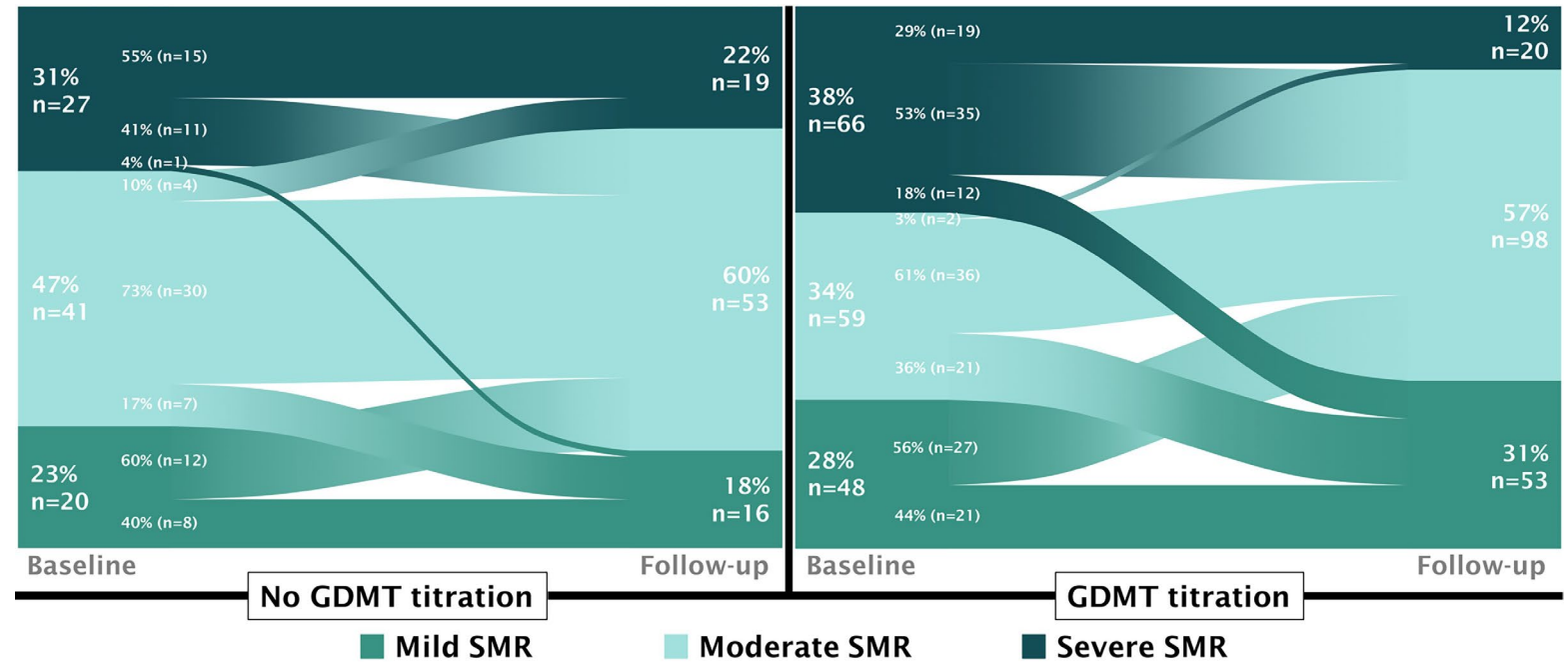
SGLT-2 Inhibitor

Replace ACE-Inhibitor with Sacubitril/Valsartan, to further improve prognosis

GDMT and reduction of SMR

- 261 patients who completed two visits with an echocardiographic exam available within 1 month at each visit

- **SMR severity improved by at least 1° in 39.3% of patients with subsequent titration of GDMT**

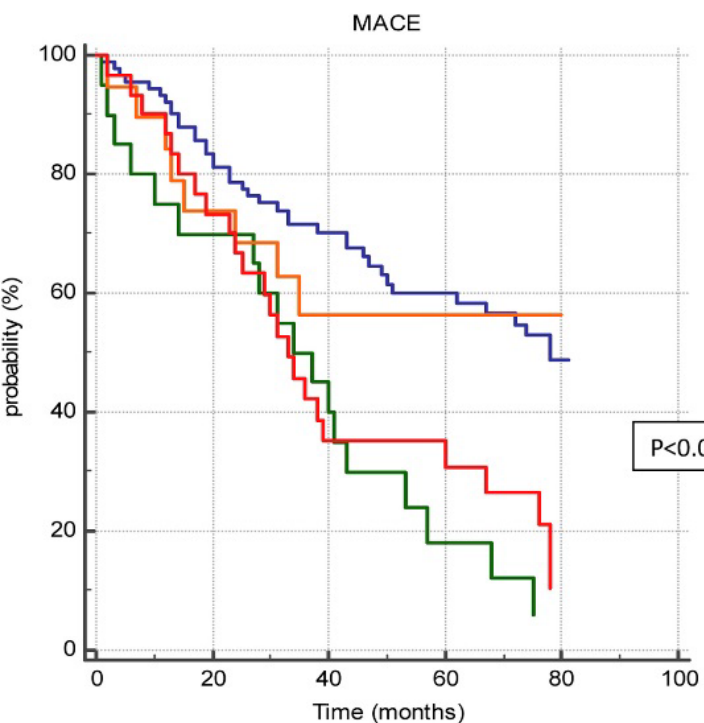


Spinka G et al. EHJ Cardiovas Imag 2022

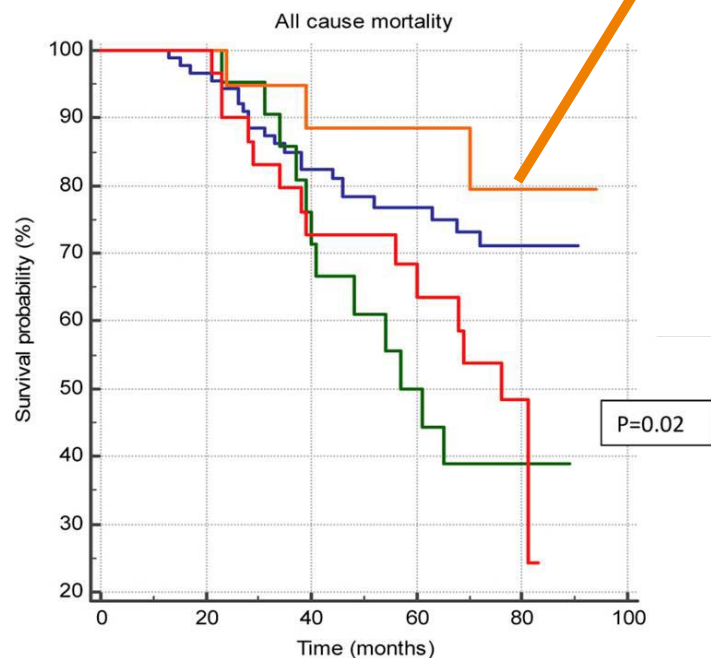
Reduction of FMR with OMT is associated with better prognosis

Patients that improved from severe to non-severe FMR

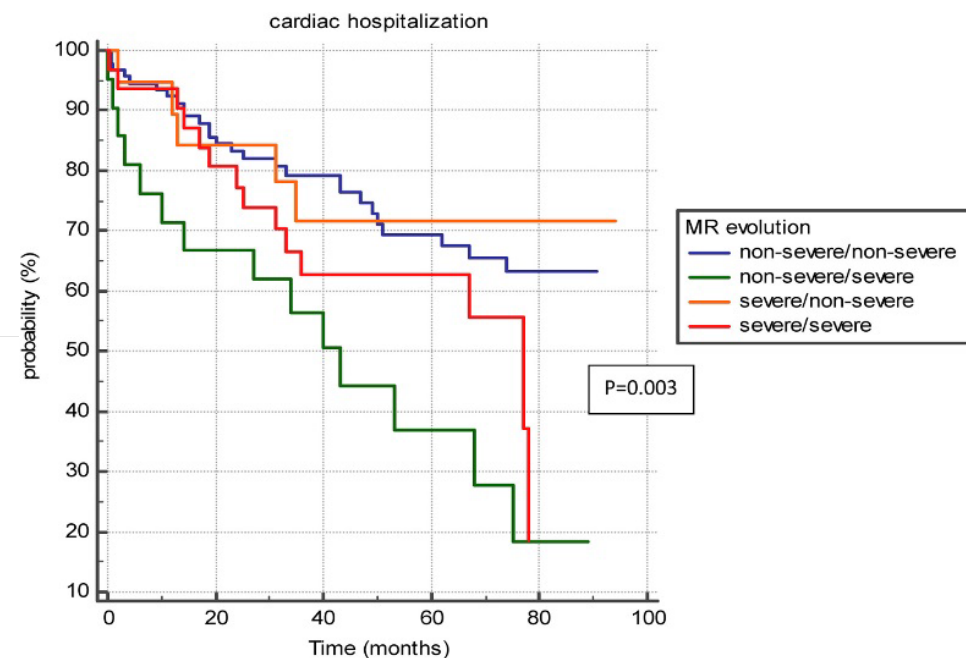
MACE



All cause mortality



Cardiac hospitalization



163 consecutive HFrEF patients (EF<40%), median FU 50months.

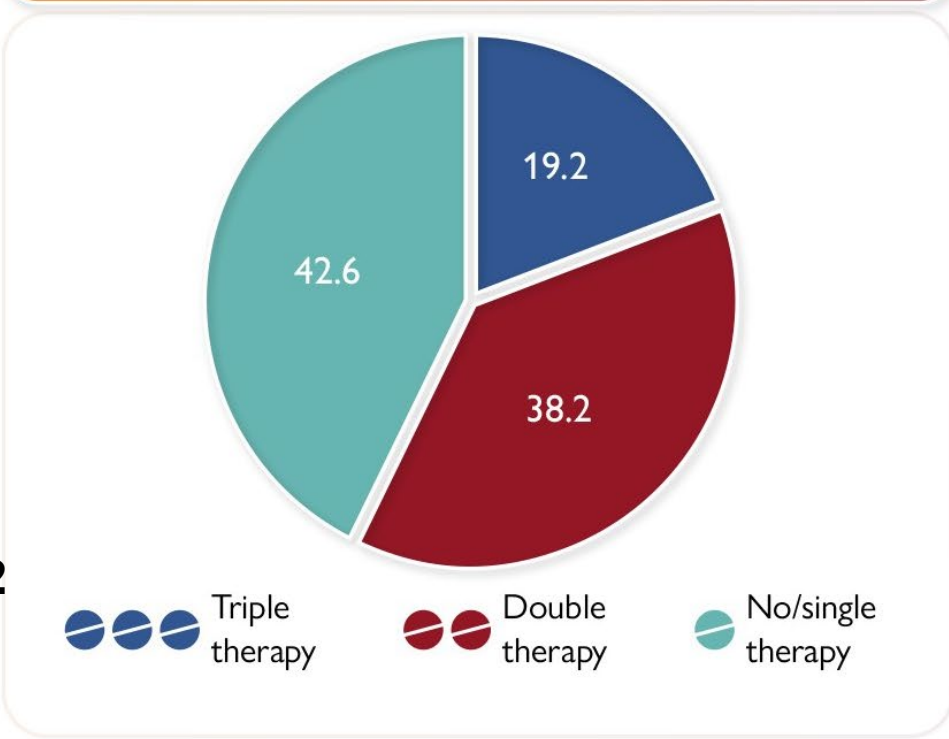
Unfortunately, most patients do not receive adequate drug therapy before mitral valve intervention....

4199 patients. 2019-2022

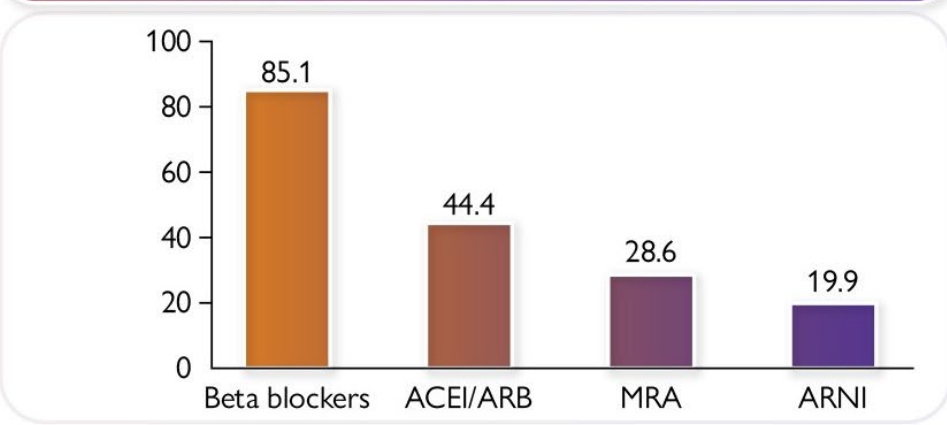
triple and double therapy before M-TEER were independently associated with reduced risk of mortality or HFH 1 year after intervention

Varshney AS et al, EHJ 23

Pre-MTEER GMT utilization (N=4199; 449 Sites)

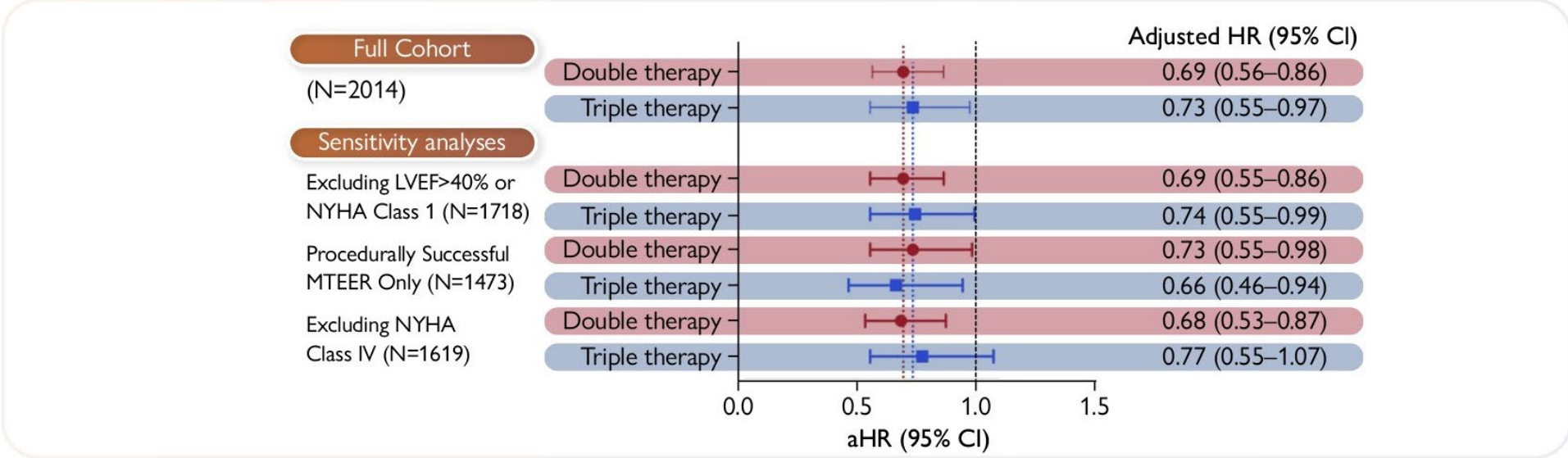


Pre-MTEER prescription rates (N=4199; 449 Sites)

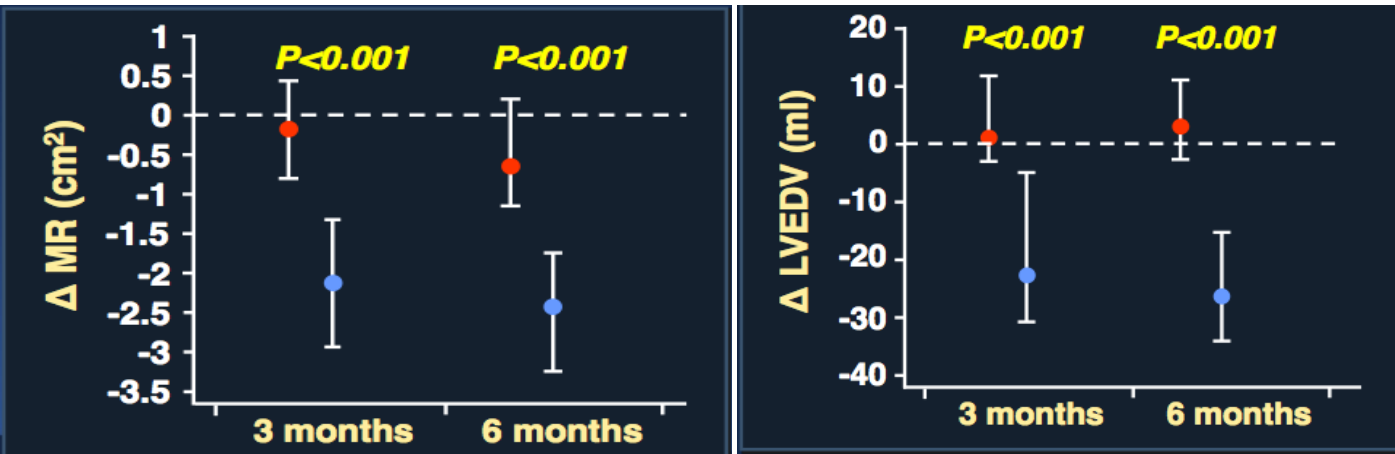


Center-level pre-MTEER triple GMT rates

- (N=144 sites performing 10+ MTEER annually)
- Range: 0-61%
 - 10 sites with 0% triple therapy use
 - ~1.5-fold variation in the likelihood that similar patients at 2 random sites were prescribed triple therapy

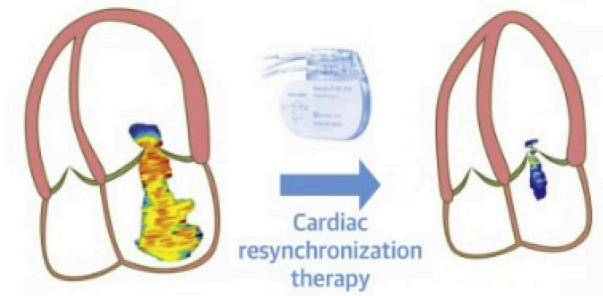


MIRACLE: CRT improves mitral regurgitation



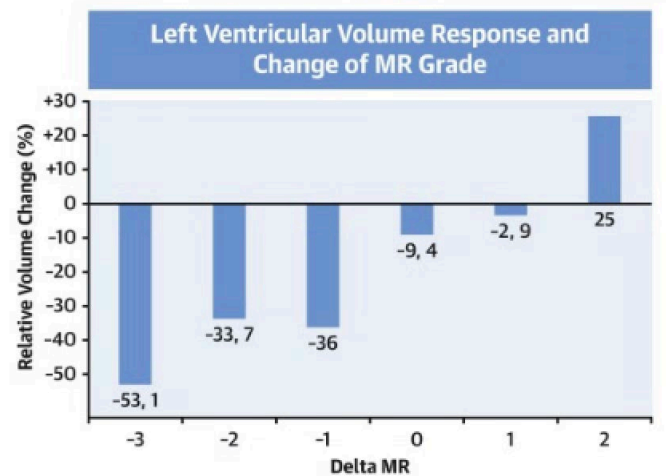
450 pts with LVEF < 35% and QRS > 130 sec

Sutton J et al, Circulation 2007

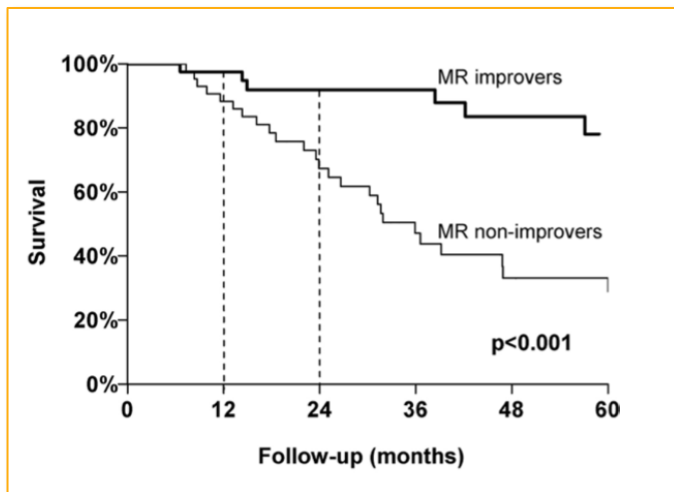


Reduction of MR after CRT and remodeling

Michalski B et al. JACC Imaging 2022

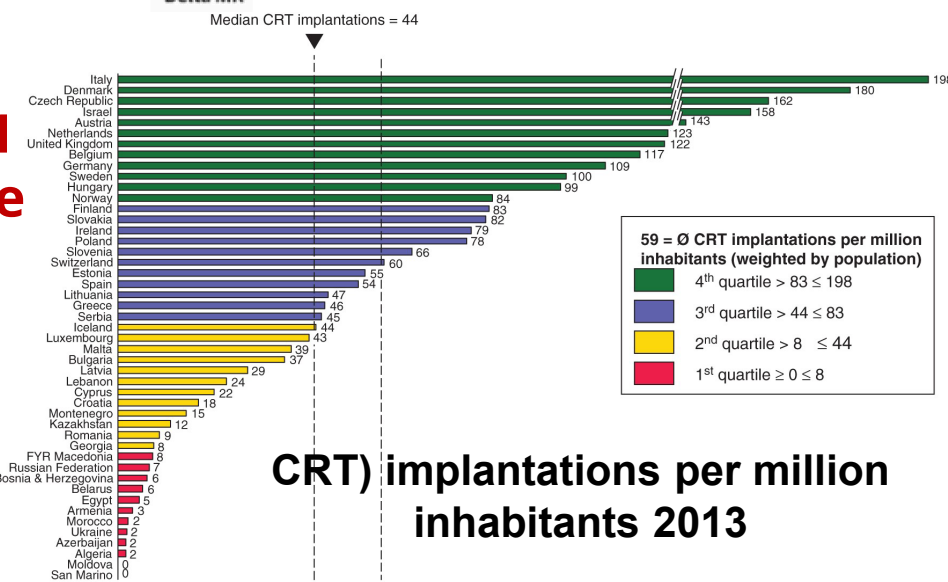


As MR improves with CRT, the prognosis also improves

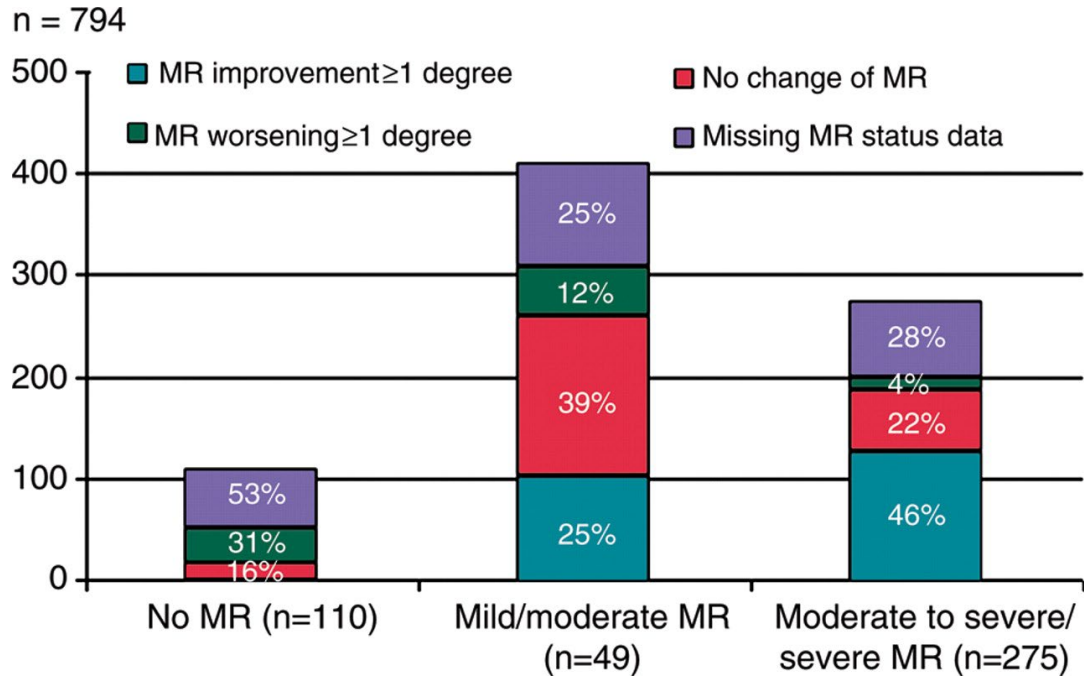


Van Bommel Circulation 2011

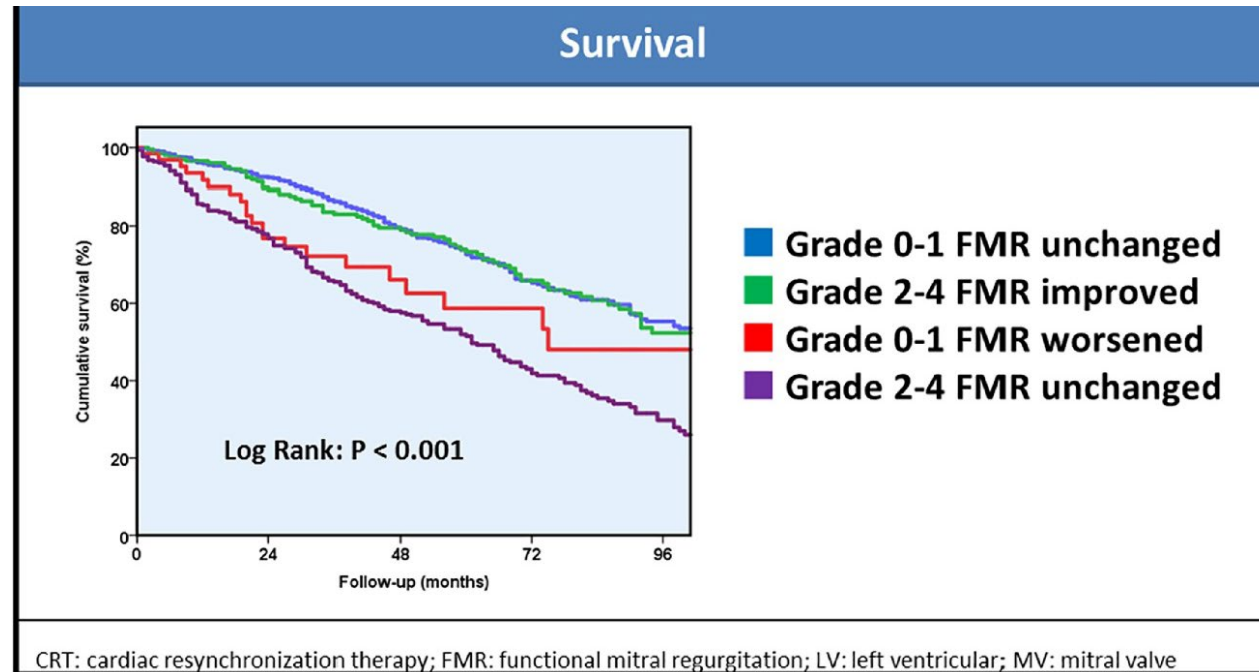
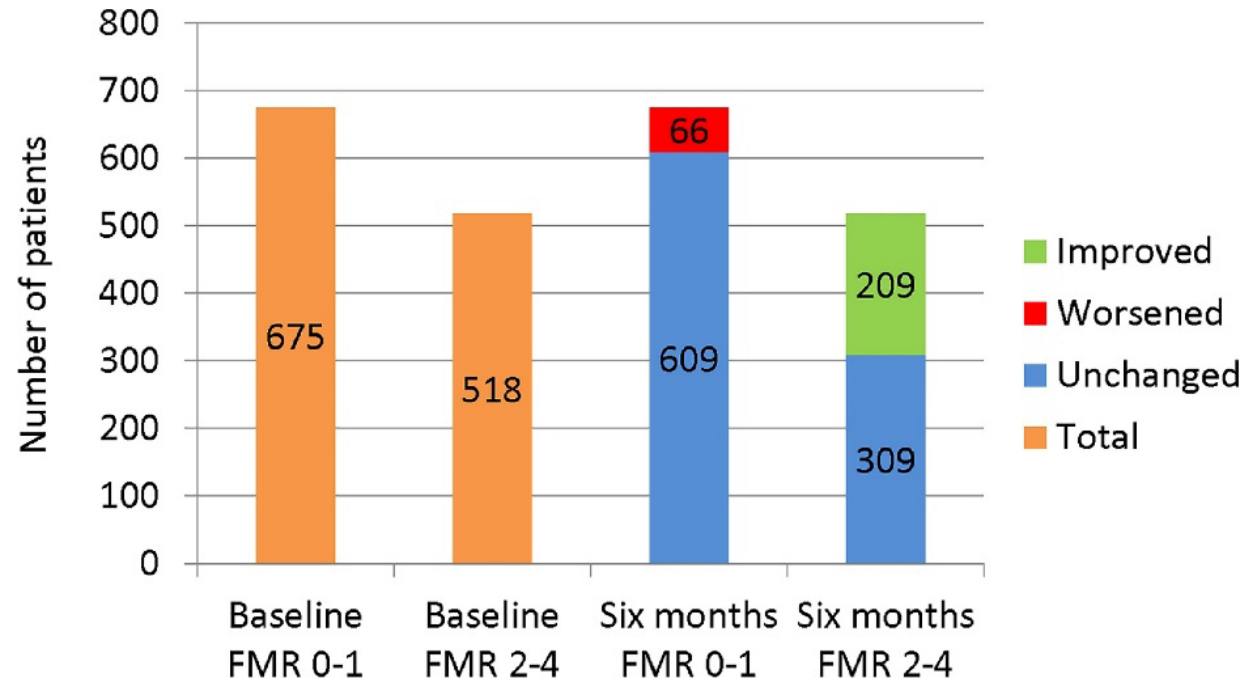
BUT: Only 1 in 3 suitable patients also gets a CRT



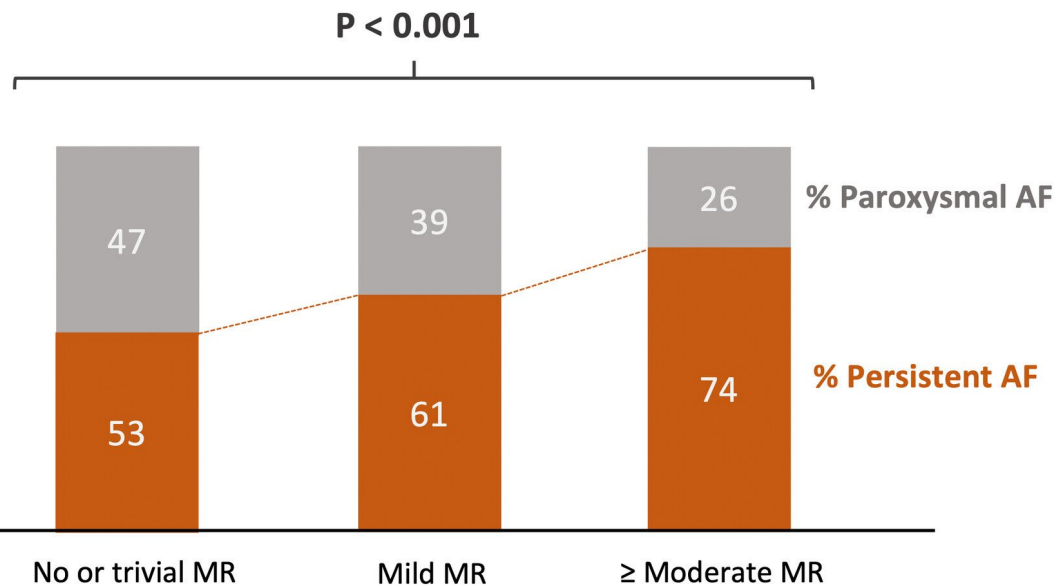
Effect of CRT on FMR and prognosis



Di Biase L et al, Europace 2011



Patients with AF and MR may benefit from ablation

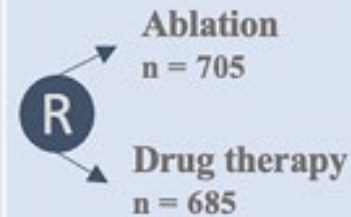
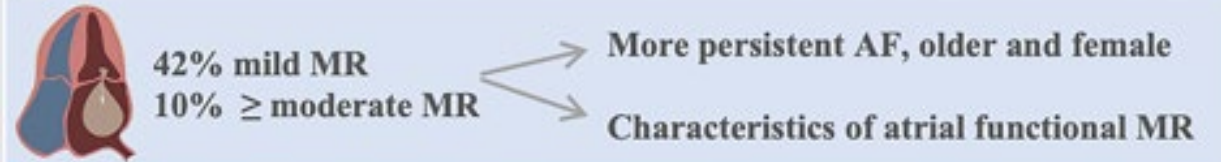


Dhont, S et al, EJHF 2025

Population



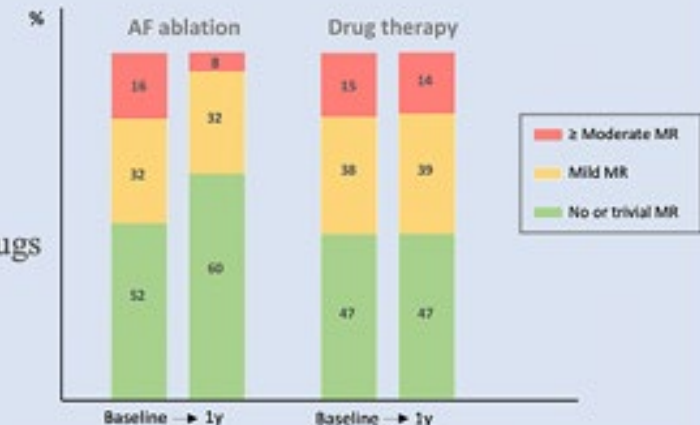
Findings



- Effect of baseline MR on ablation vs drugs**
- No effect on death/hospitalization (p= 0.115)
 - Better symptom control (CSS-AF & NYHA, p<0.001)
 - Less AF recurrence (p<0.001)

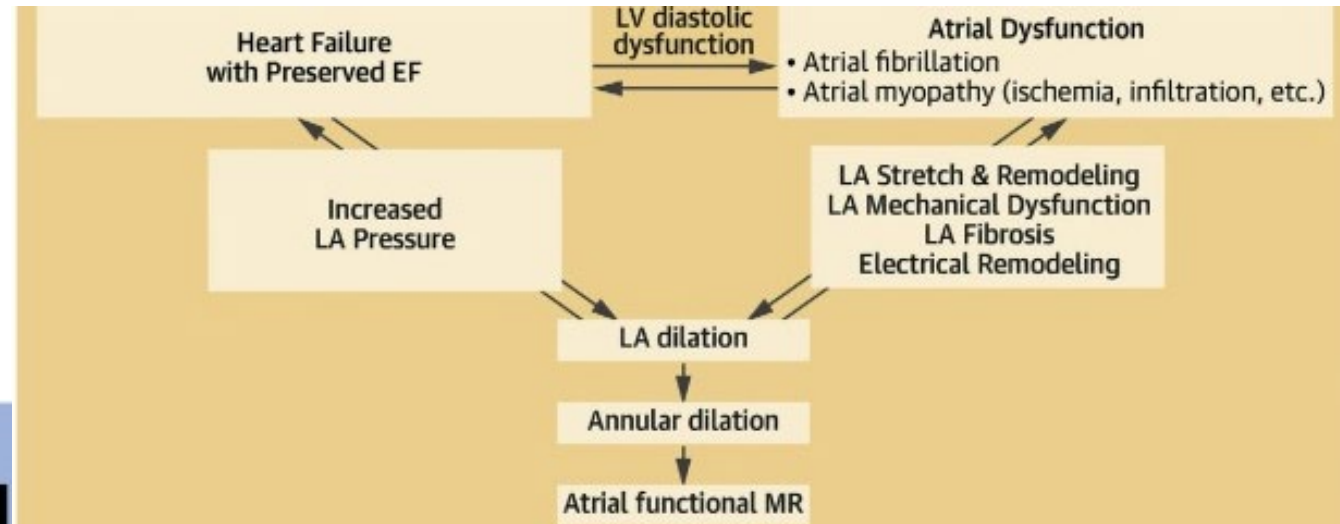
MR evolution after 1 year (n=248)

Ablation reduced MR more than drugs (OR 0.69, p-interaction = 0.040)



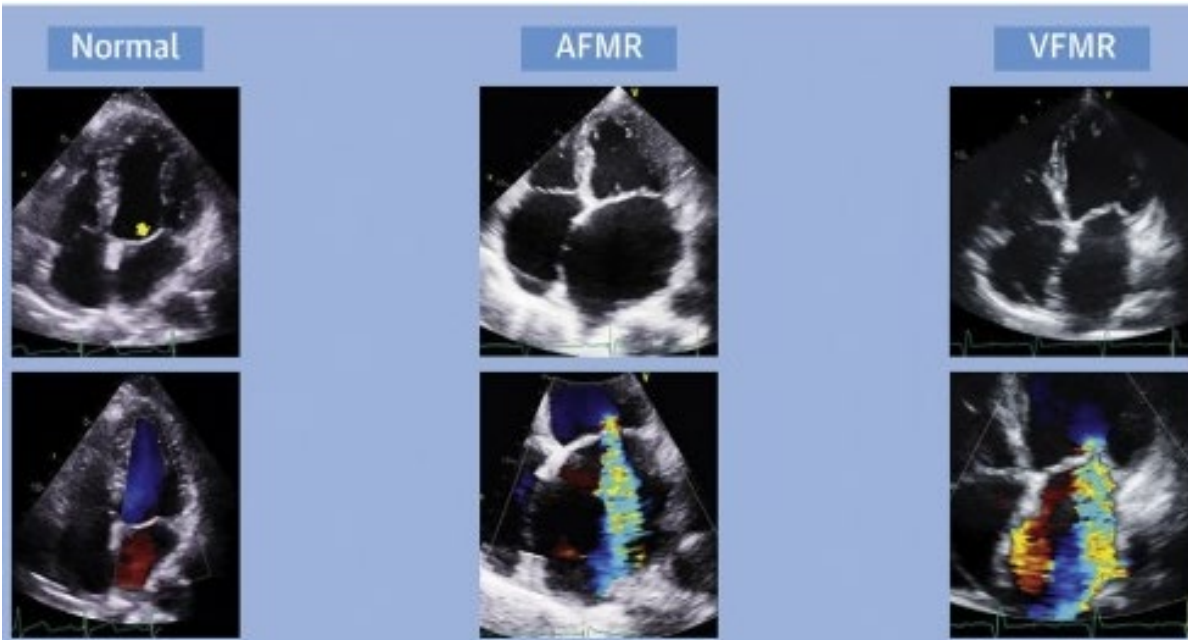
HFpEF and SMR:

(Atrial functional Mitral regurgitation)



Criteria	Isolated AFMR	Isolated VFMR
LV size & geometry	<ul style="list-style-type: none"> Normal by definition (LV size may dilate secondarily in later stages of significant AFMR) Preserved LV shape 	<ul style="list-style-type: none"> Often dilated (but not necessarily). Often increased LV sphericity
LV systolic function	<ul style="list-style-type: none"> Preserved regional and global function Peak LV GLS preserved (16-18%) or mildly reduced 	<ul style="list-style-type: none"> Either global LV systolic dysfunction or focal wall motion abnormalities Peak LV GLS typically reduced ($\leq 16\%$)
LA size	<ul style="list-style-type: none"> Dilated by definition LAVI usually moderately or severely enlarged (≥ 40 mL/m²) 	<ul style="list-style-type: none"> Often dilated
Annular size	<ul style="list-style-type: none"> Dilated by definition Sys D_{AP} > 35 mm in PLAX or, Sys D ≥ 36 mm in 4-Chamber or, 3D Mid-sys AA > 7.0 cm²/m² Annular flattening 	<ul style="list-style-type: none"> Often dilated in response to LA dilation Annular flattening
Leaflet morphology	<ul style="list-style-type: none"> Macroscopically normal appearance At most mild leaflet thickening 	<ul style="list-style-type: none"> Macroscopically normal appearance Variable leaflet thickening
Leaflet motion	<ul style="list-style-type: none"> Usually normal (Carpentier type I MR) 	<ul style="list-style-type: none"> Restrictive (Carpentier type IIIb MR)
Leaflet coaptation point	<ul style="list-style-type: none"> At annular level or mildly displaced apically 	<ul style="list-style-type: none"> Displaced apically (sub-valvular tethering)
MR jet direction	<ul style="list-style-type: none"> Usually central but may be eccentric 	<ul style="list-style-type: none"> Eccentric or central

= HFpEF



Zoghbi WA et al, JACC Cardiol Img. 2022

ARNI in HFpEF and secondary MR – PRAISE-MR trial

The PRAISE-MR trial

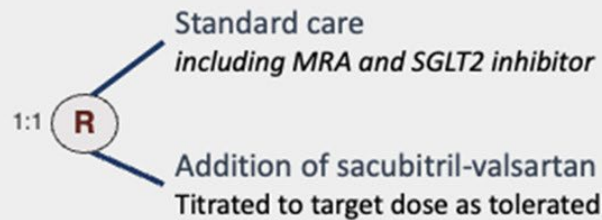
A multicenter, investigator-initiated, open-label, randomized trial with blinded endpoint assessment (PROBE design)

Population (n = 110)

Adults with heart failure with preserved ejection fraction
 NYHA functional class \geq II
 \geq moderate atrial FMR documented within the past year



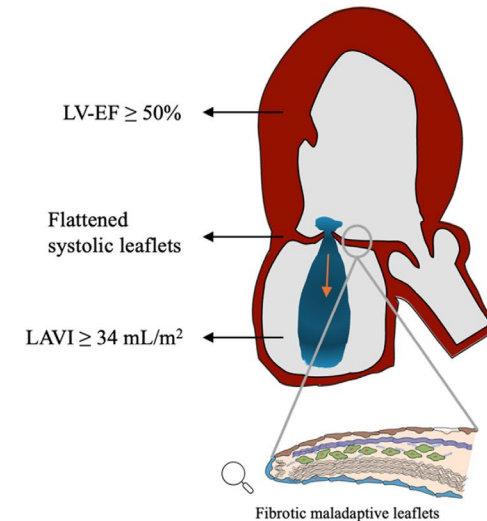
Intervention



CPETechno
 KCC Questionnaire
 Biomarkers (NTproBNP)
 24-hour BP monitoring

Outcomes

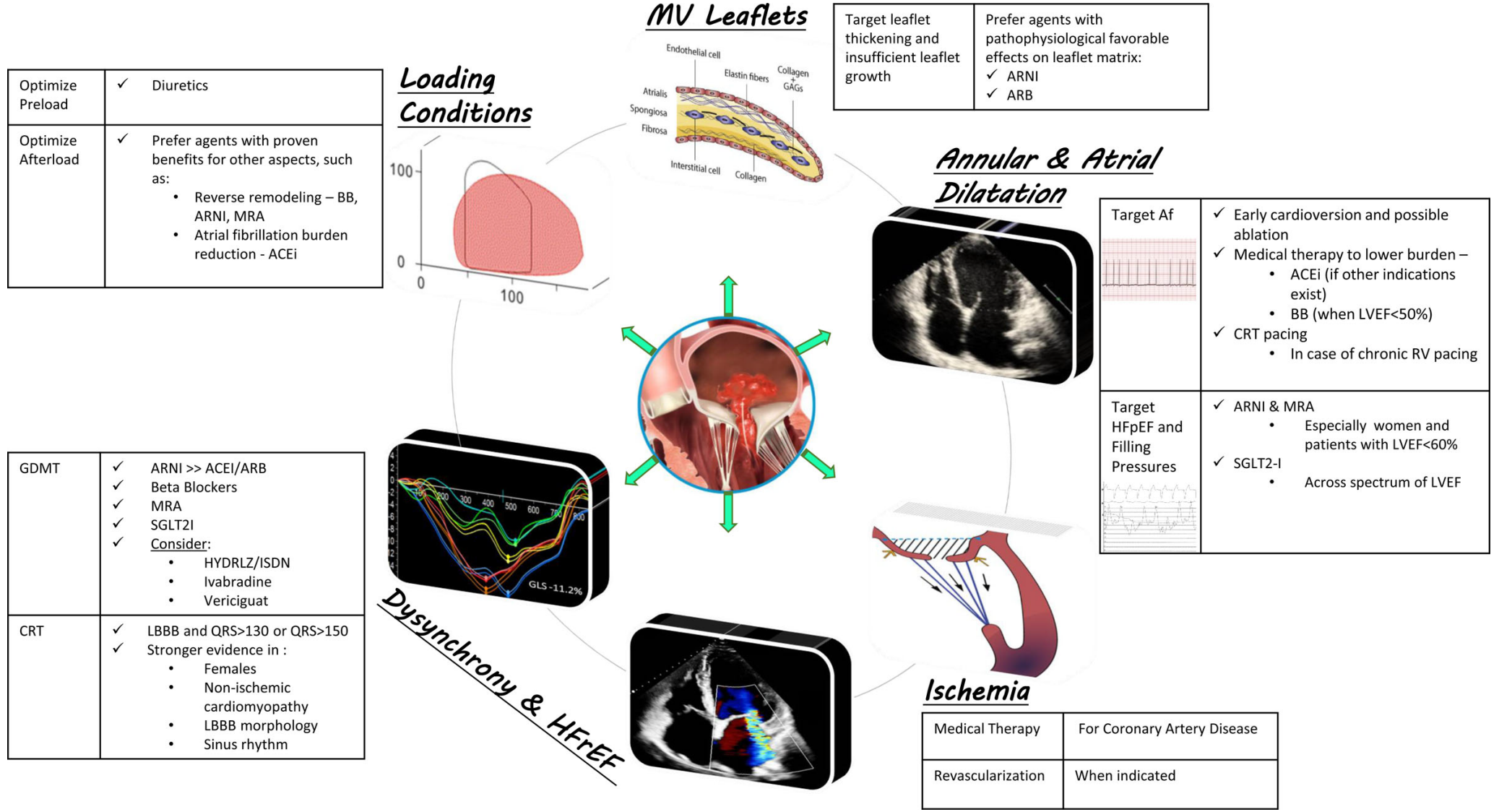
Primary:	Change in mPAP/CO slope
Secondary:	Atrial FMR severity LA volume and function
	NTproBNP levels KCC Questionnaires
	Peak VO_2 VE/ VCO_2 slope



Potential Modes of Action Sacubitril/Valsartan

- LA remodeling (\uparrow function, \downarrow size)
- \downarrow Afterload and preload (vasodilation and diuresis)
- Leaflet adaptation (\downarrow stiffness and thickening)

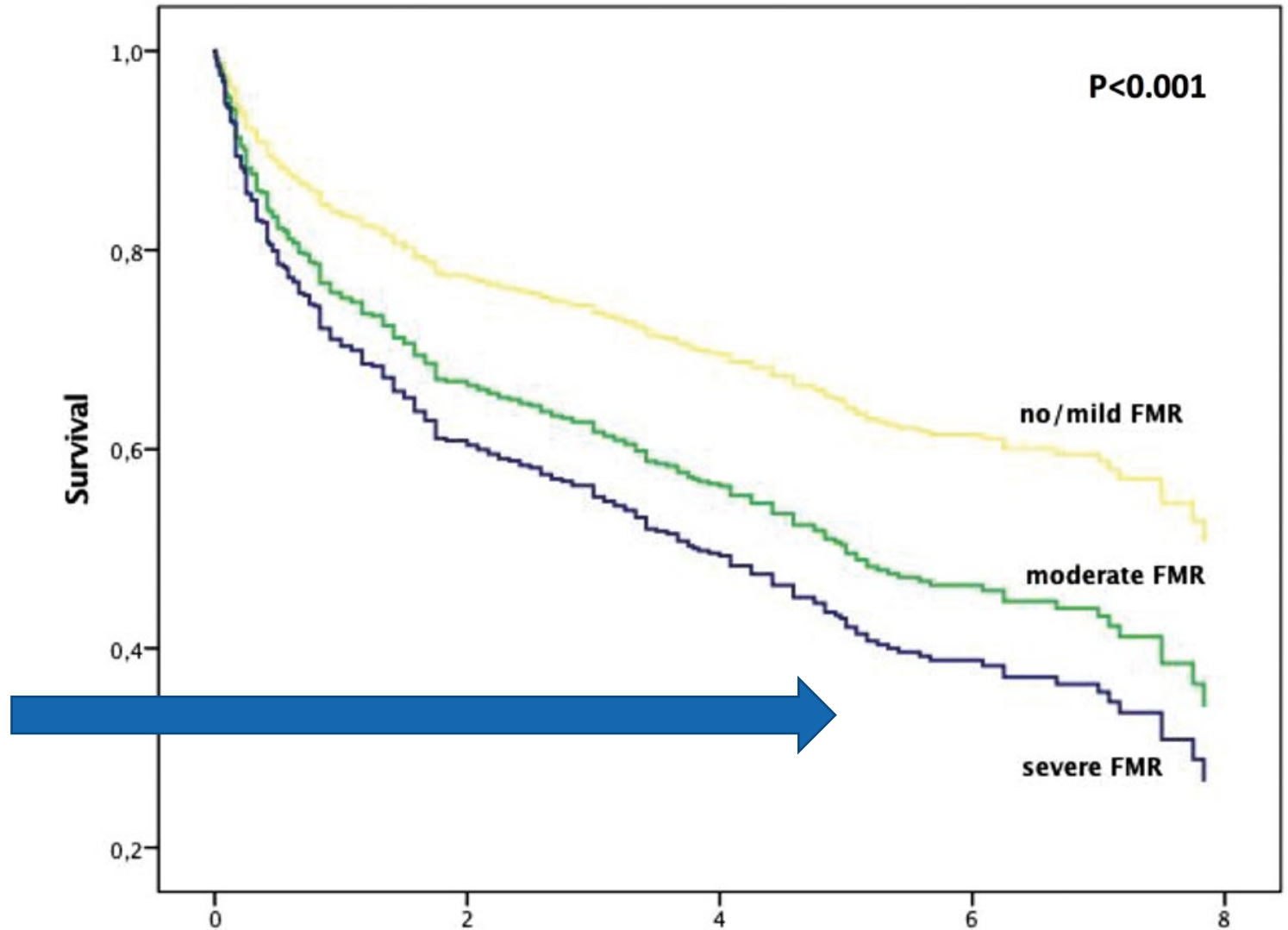
Targeted therapies for secondary mitral regurgitation



Persistence of severe FMR under OMT has bad prognosis

576 consecutive HFrEF patients
 Median FU 62 month: 47% of patients died

1. Adverse prognostic impact of severe FMR remains despite OMT
2. Severe FMR was associated with poor outcome particularly in in intermediate-failure phenotype of HFrEF (NYHA II/III, moderately reduced EF and within the second quartile of NTproBNP (871-2360pg/ml))

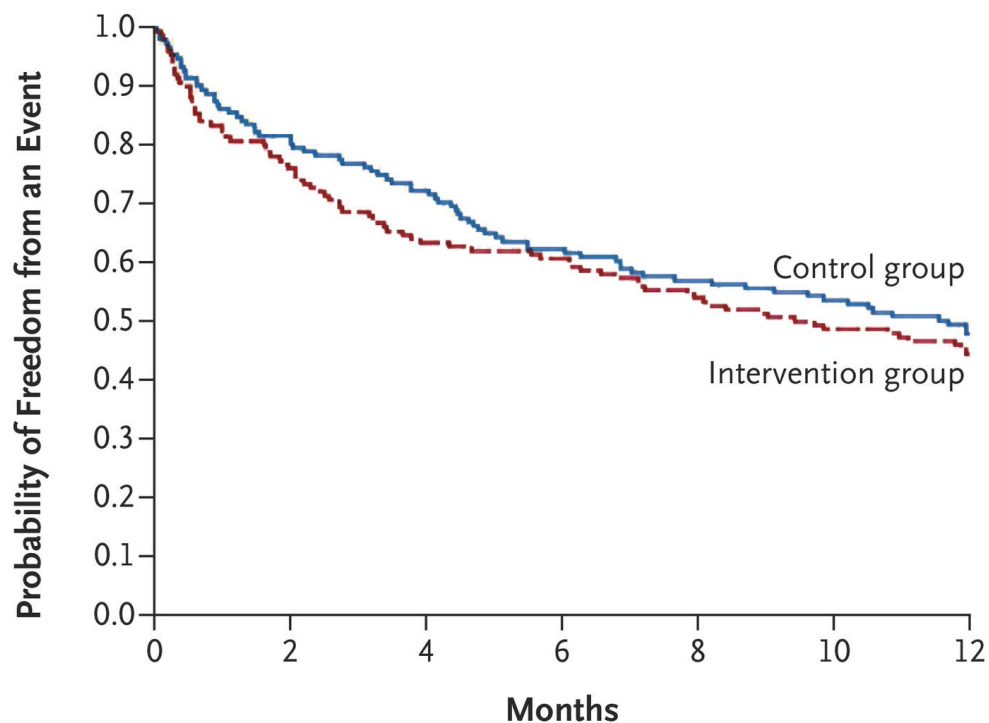


n	Years				
No/mild FMR	272	209	173	56	12
Moderate FMR	185	120	87	39	8
Severe FMR	119	61	42	22	3

Goliasch G et al, EHJ 2018

7 years ago: TEER in FMR

Mitra.fr – «Neutral»

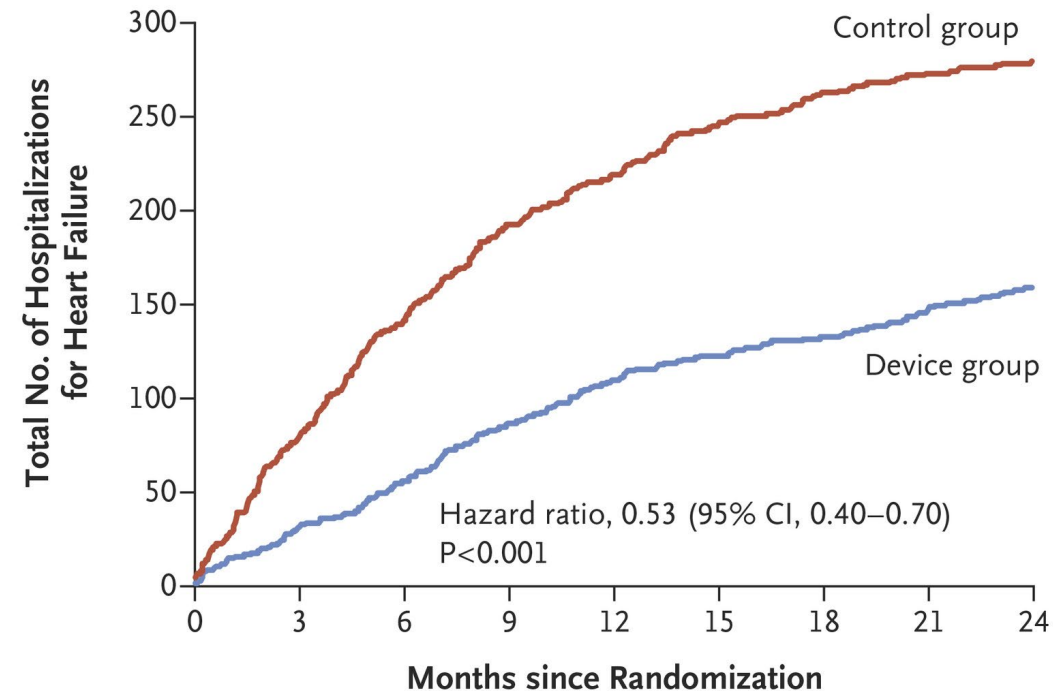


No. at Risk	0	2	4	6	8	10	12
Control group	152	123	109	94	86	80	73
Intervention group	151	114	95	91	81	73	67

Obadia JF et al NEJM 2018

COAPT – «Revolution»

A Hospitalization for Heart Failure



No. at Risk	0	3	6	9	12	15	18	21	24
Control group	312	294	271	245	219	176	145	121	88
Device group	302	286	269	253	236	191	178	161	124

Stone G et al NEJM 2018

RESHAPE-HF2 Trial – HFrEF and Secondary Mitral Regurgitation

Randomized, controlled (**no sham control**) moderate to severe MR. 1:1 M-TEER with GDMT or GDMT only

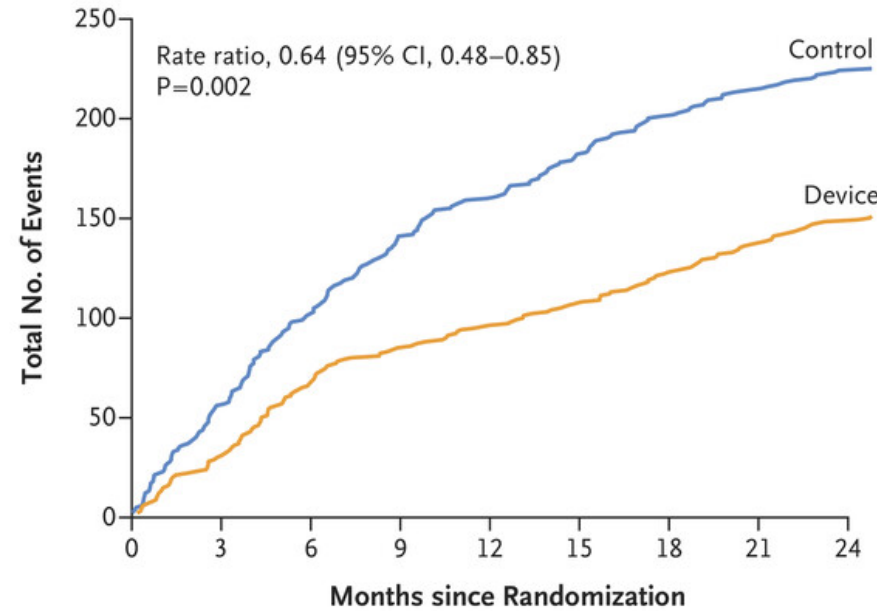
3 primary endpoints:

- «rate of the composite of first or recurrent hospitalization for HF or CV death»
- «rate of first or recurrent hospitalization for HF»
- «QOL change form baseline to 12 months»

Characteristics:

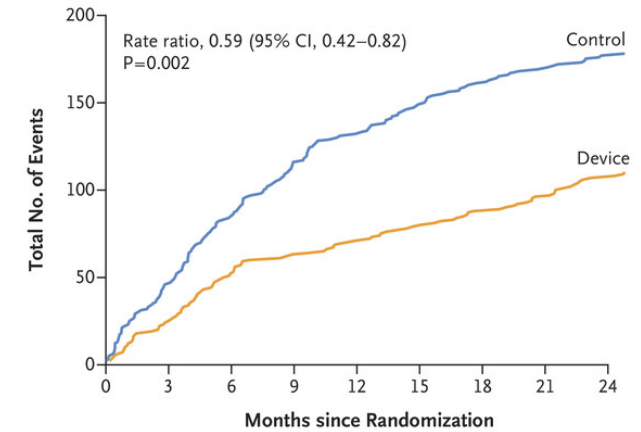
- 70 years old, 80% male, 35% DM, 50% hypertension, 48% Afib
- Non-ischemic HF 35%
- NYHA III 60%
- HFrEF within 1 year 66%
- NTproBNP 2700ng/ml, SBP 112mmHg, GFR 55ml/min
- **LVEF 32%, LVEDV 200ml, medium regurgitant volume 35ml**
- BB 95%, ACE, ARB or ARNI: 82%, MRA 80%, SGLT2 9%

A Composite of Hospitalization for Heart Failure or Death from Cardiovascular Causes



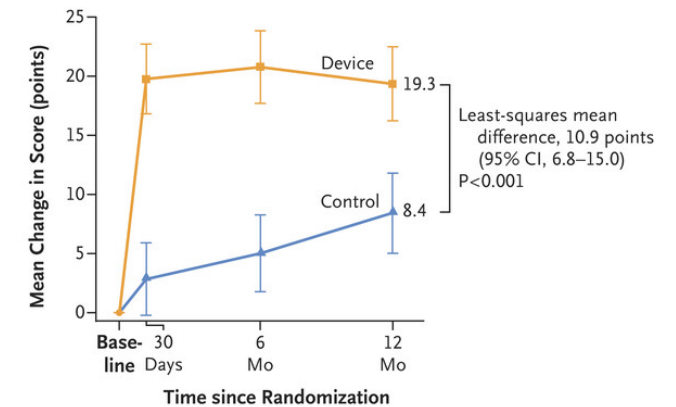
No. at Risk	0	3	6	9	12	15	18	21	24
Control	255	240	223	204	189	179	165	155	146
Device	250	241	222	207	197	191	179	170	163

B Hospitalization for Heart Failure



No. at Risk	0	3	6	9	12	15	18	21	24
Control	255	240	223	204	189	179	165	155	146
Device	250	241	222	207	197	191	179	170	163

C KCCQ-OS Score



RESHAPE-HF2 - Percutaneous repair of moderate-to-severe or severe functional mitral regurgitation...

Secondary Endpoints

Secondary end points	Device	GDMT only		
Mitral regurgitation grade $\leq 2+$ at 12 mo — no./total no. (%)	132/146 (90.4)	43/119 (36.1)**	21.3 (10.7–45.8) ^{††}	<0.001 [¶]
Mean change in 6-min walk distance from baseline to 12 mo — m	34.0 \pm 105.9	5.1 \pm 97.6	20.5 (0.3–40.7)	0.05 ^{‡‡}
Rate of death from any cause during the complete* follow-up per 100 patient-yr (no. of events/total no. of patient-yr)	17.0 (142/836.7)	18.6 (142/765.2)	0.90 (0.71–1.13)	0.37
Rate of recurrent hospitalization for any cause during 24 mo per 100 patient-yr (no. of events/total no. of patient-yr)	48.7 (199/408.6)	61.0 (233/381.9)	0.82 (0.63–1.07)	0.15
NYHA functional class I or II heart failure at 12 mo — no./total no. (%) ^{§§}	140/188 (74.5)	96/164 (58.5)	2.35 (1.48–3.77) ^{††}	<0.001 [¶]

*Follow-up times for 24 months assessments:

- Overall: median 24.0 months (IQR 12.0–25.0); Device group: 24.2 (IQR 15.7–25.0); Control group: 23.6 (IQR 10.4–24.9).

Follow-up times for all-cause mortality assessment:

- Overall: median 29.4 months (IQR 14.0–61.1); Device group: 34.3 (IQR 16.0–63.1); Control group: 27.0 (IQR 11.6–58.0)



Stefan Anker
Germany



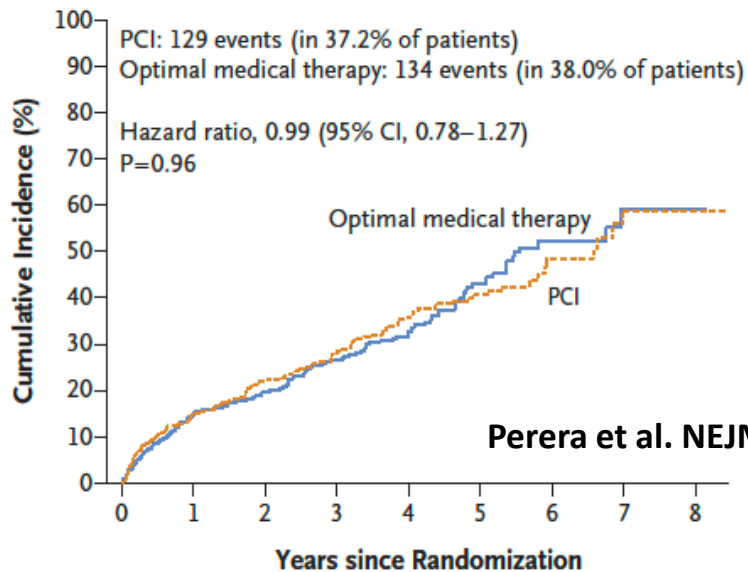
#ESCCongress

The importance of GDMT optimization in « device » trials

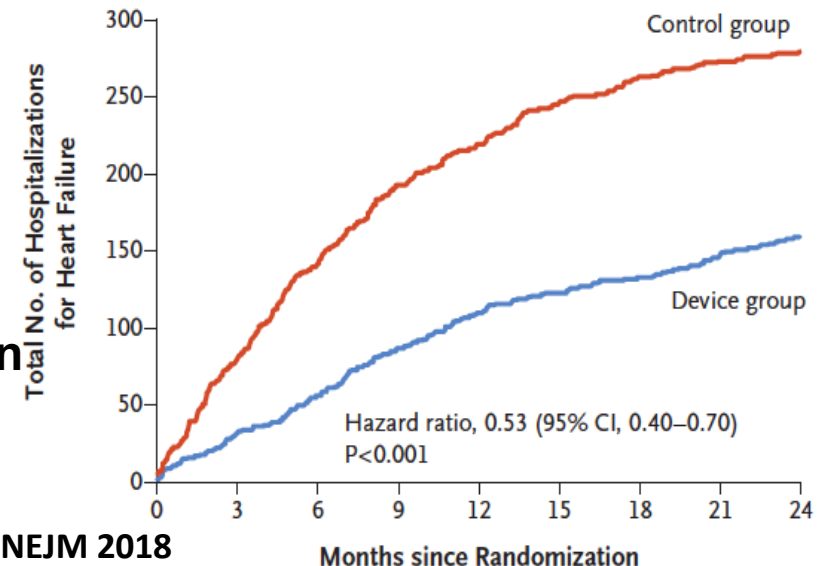


Protocol: «A medical-therapy committee reviewed guidelines periodically and refined recommendations to **ensure that the pharmacologic therapy given to all patients** in the trial **remained contemporary.** »

Protocol: « Subjects must **continue to take baseline medications without change** during follow-up (...). In general, **neurohormonal antagonists should not be changed.** »



Courtesy of N. Mewton



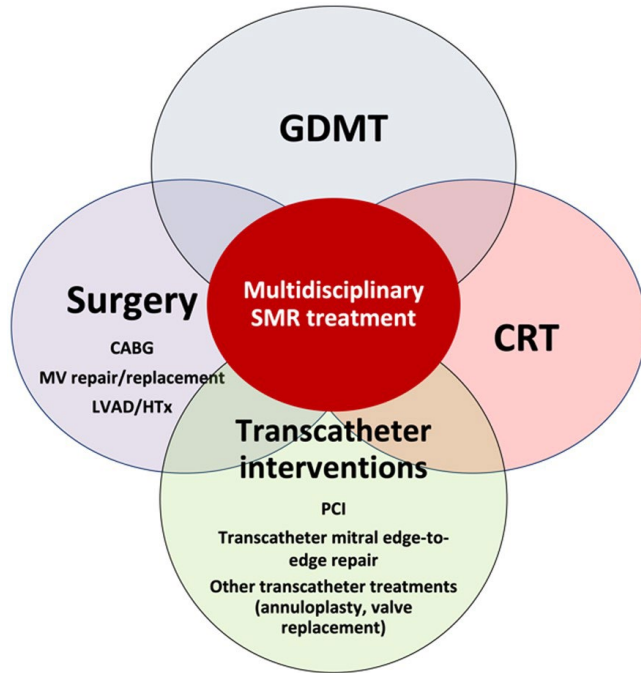
PERSONAL thoughts on M-TEER: OMT, and CRT significantly affects outcome in patients with severe sMR.

M-TEER with significant clinical benefits (hospitalization) in selected patients

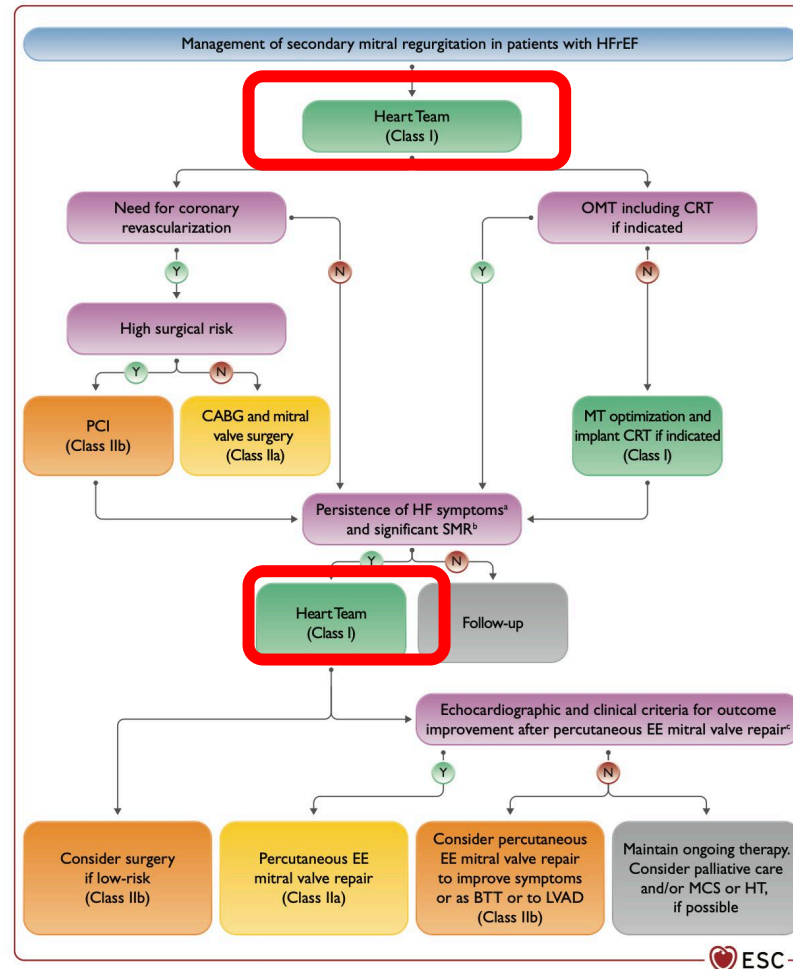
- Positive findings in RESHAPE-HF2 are driven by the number of HF and CV hospitalizations
- CAVE: **no sham control** in all the device studies
- Definition of HF and CV hospitalization may be subject of bias. Decrease in these endpoints did not translate to a decrease in all-cause hospitalization...
- in the COAPT trial, patients were very selected. Patients in the control group were not allowed to adapt GDMT during follow up
- Still few patients on Optimal medical treatment SGLT-2 inhibitor and ARNI
- We must not neglect device related complications
- We should avoid simplification and overinterpretation

Therefore, a "Heart Team" Approach is absolutely crucial

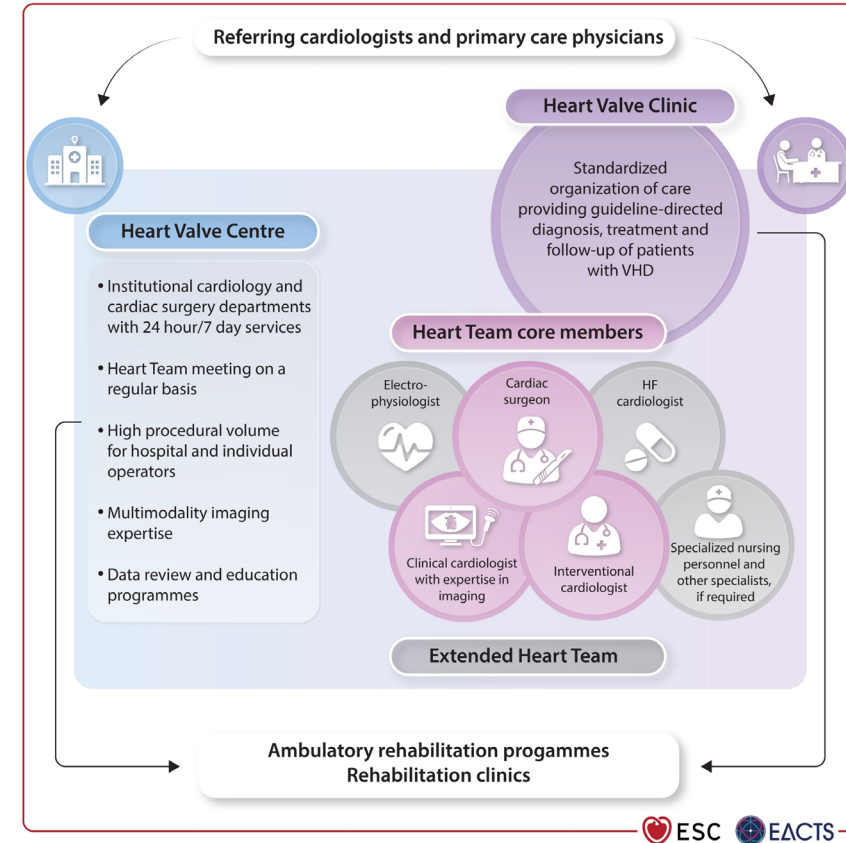
Therapy decisions only in the "heart team" with a heart failure specialist



Coats AJ et al, joint position statement from HFA, EACVI, EHRA and EAPCI, EHJ 2021



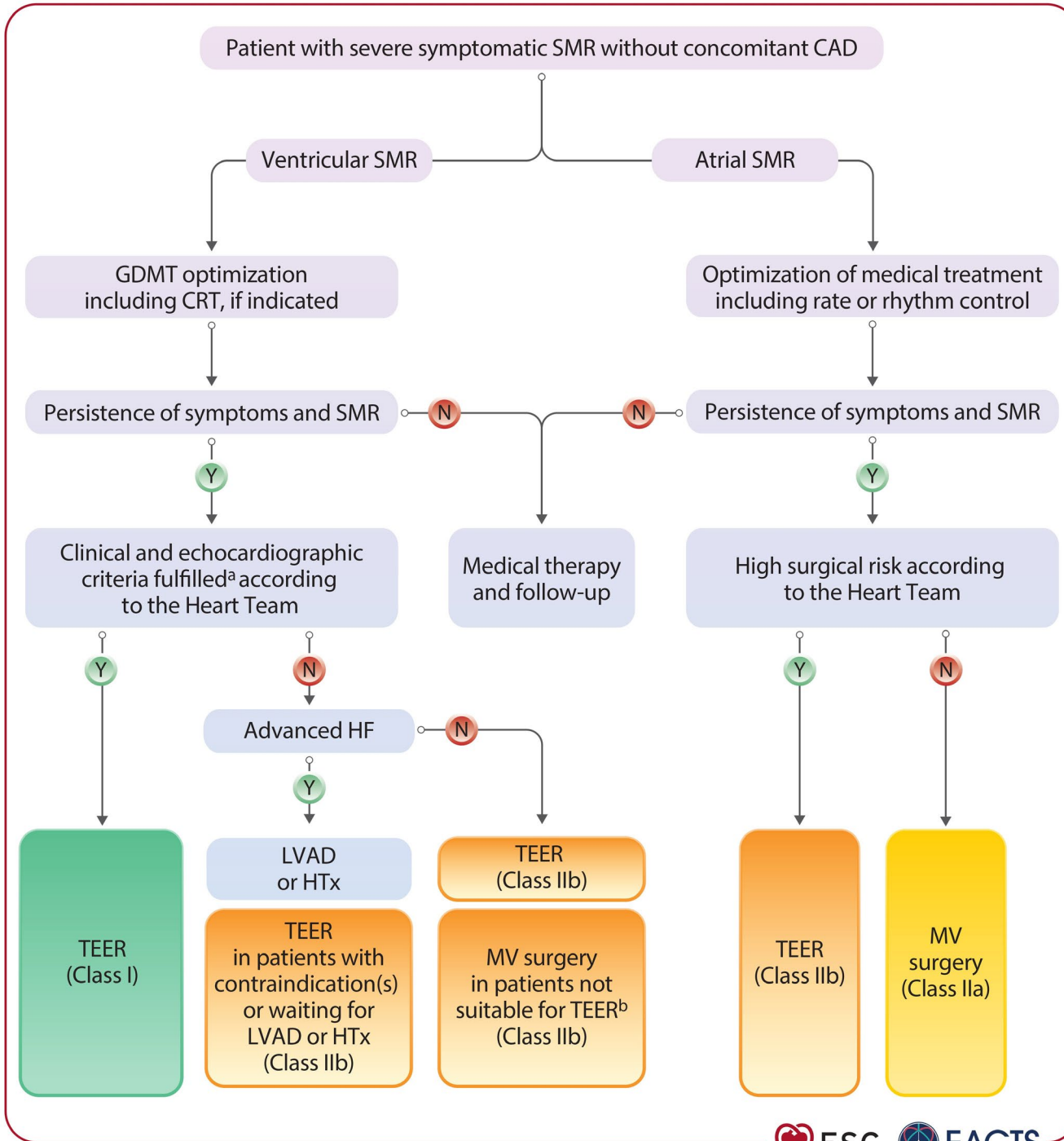
HF ESC Guidelines 2021



Valve Guidelines ESC 2025

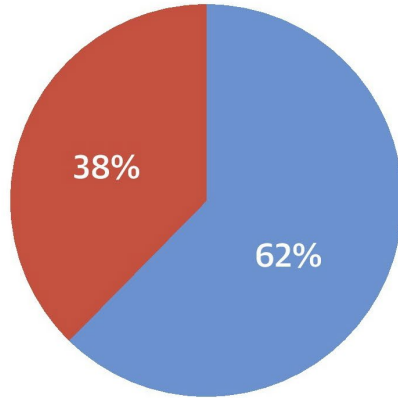
Class IA recommendation for M-TEER....

- Anatomy deemed suitable for M-TEER
- NYHA class \geq II
- LVEF 20%–50%
- LVESD \leq 70 mm
- At least one HF hospitalization within the previous year or increased natriuretic peptide levels (BNP \geq 300 pg/mL or NT-proBNP \geq 1000 pg/mL)
- SPAP \leq 70 mmHg
- No severe RV dysfunction
- No Stage D or advanced HF
- No CAD requiring revascularization
- No severe AV and/or TV disease
- No hypertrophic, restrictive, or infiltrative cardiomyopathies



Impact on outcomes of GDMT uptitration after M-TEER

GDMT Uptitration After M-TEER

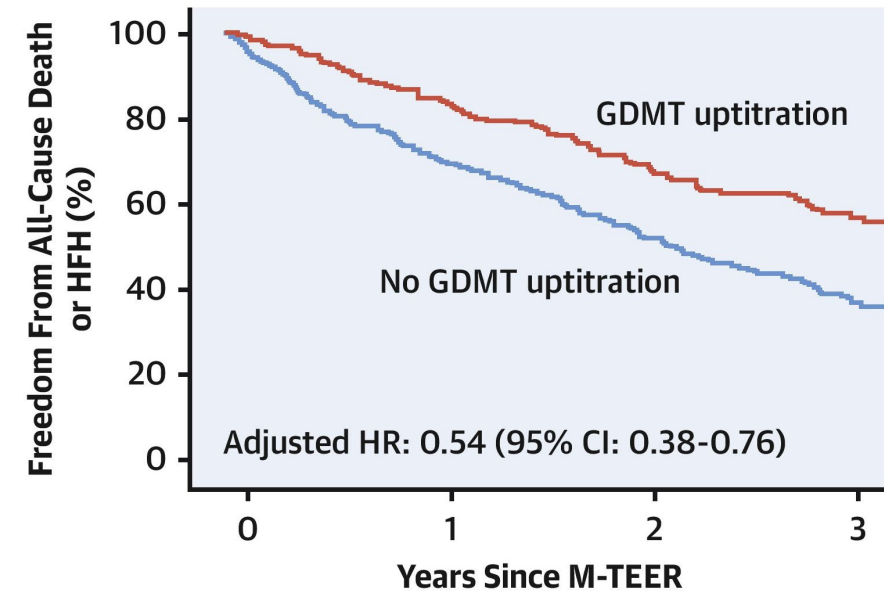
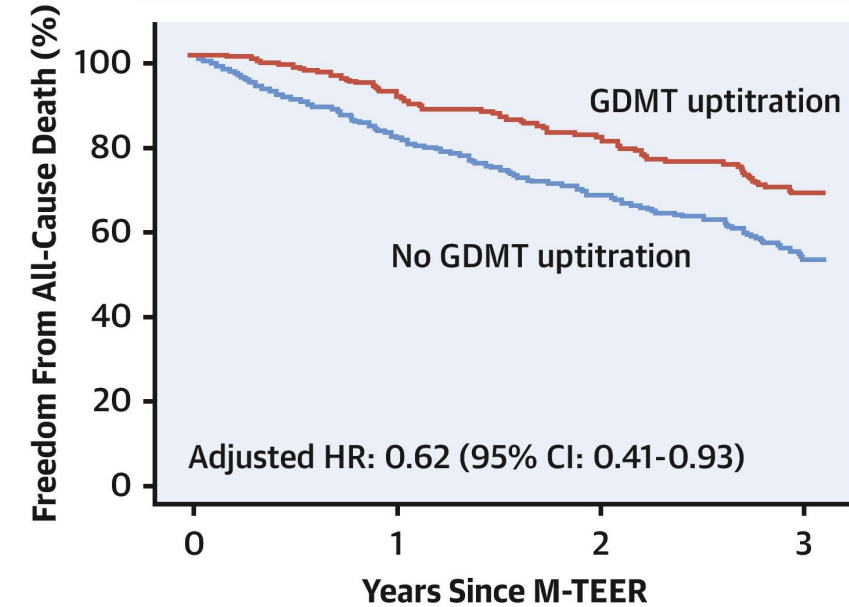


■ No uptitration ■ Uptitration

Predictors of GDMT Uptitration

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 Uptitration and Outcomes



Adamo M et al, JACC Intv 2023

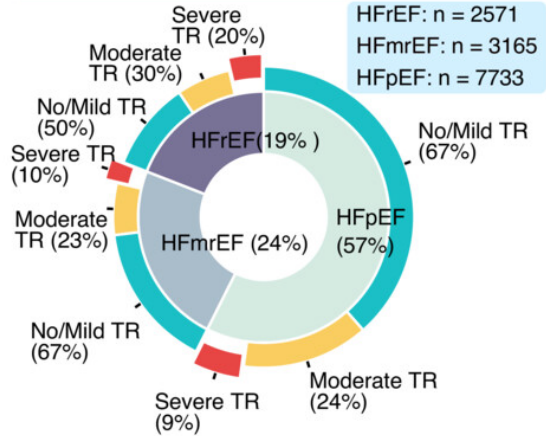
Tricuspid valve

Moderate and severe functional TR is common in all HF subtypes

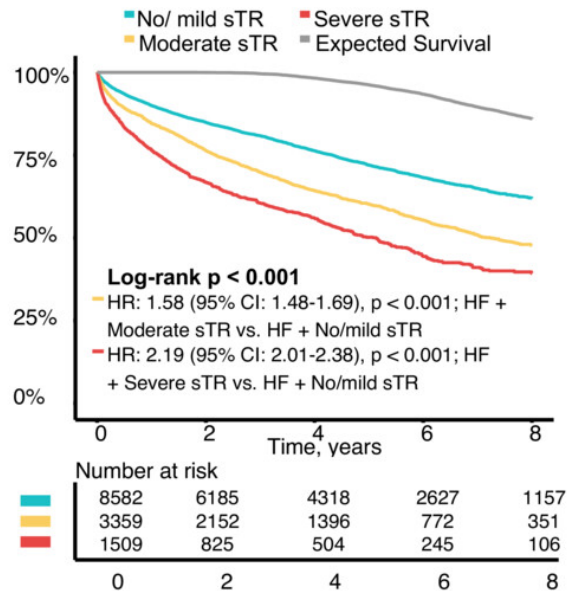
With increasing severity of TR – increase in mortality, regardless of HF subtype

HFpEF is often associated with secondary TR – However, the underlying LV pathology is often missed, and heart failure symptoms are incorrectly attributed to TR

Prevalence of sTR in the community



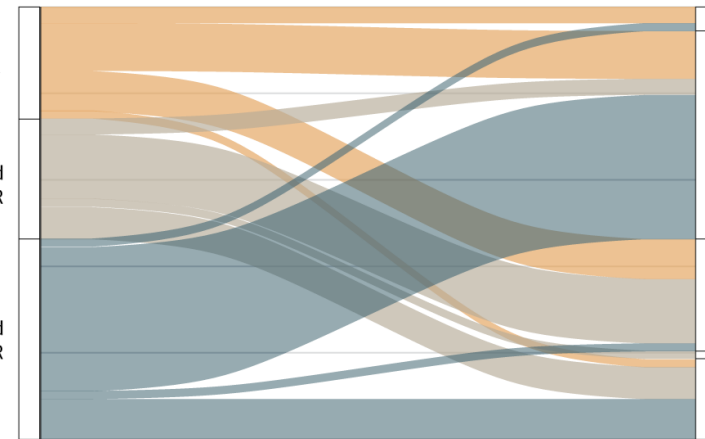
Long-term survival (2010-2020)



Treatment of sTR

- **Low-overall** treatment utilization despite **low barrier** healthcare access
- Interventions equally **rare** in **all HF subtypes**
- **RCTs** are needed to **assess survival benefit** of sTR correction

Echocardiography



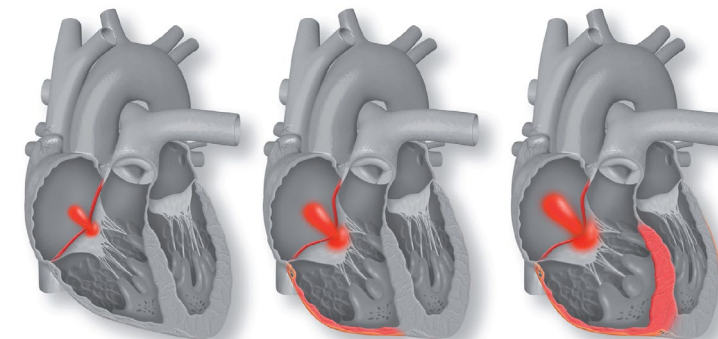
Echocardiography + RHC

- A-STR without PH (n=3)
- HFpEF with combined precapillary and postcapillary PH (n=26)
- HFpEF with isolated postcapillary PH (n=14)
- Isolated V-STR (n=1)
- Precapillary PH (n=10)
- Group 3: n=3

HFpEF

TR classification

- Secondary Tricuspid Regurgitation
- HFpEF / HFmrEF / HFrfEF



Phase I

- Increased RV systolic pressure
- sPAP ↑
- RV dilatation
- TV annular dilatation

Phase II

- Progressive RV dilatation
- RA dilatation
- TV annular dilatation

Phase III

- RV dilatation and distortion
- sPAP ↑
- RA dilatation
- TV annular dilatation
- Tethering of TV leaflets

Heitzinger G et al, EJHF 2023

Bartko PE et al, EHJ 2020

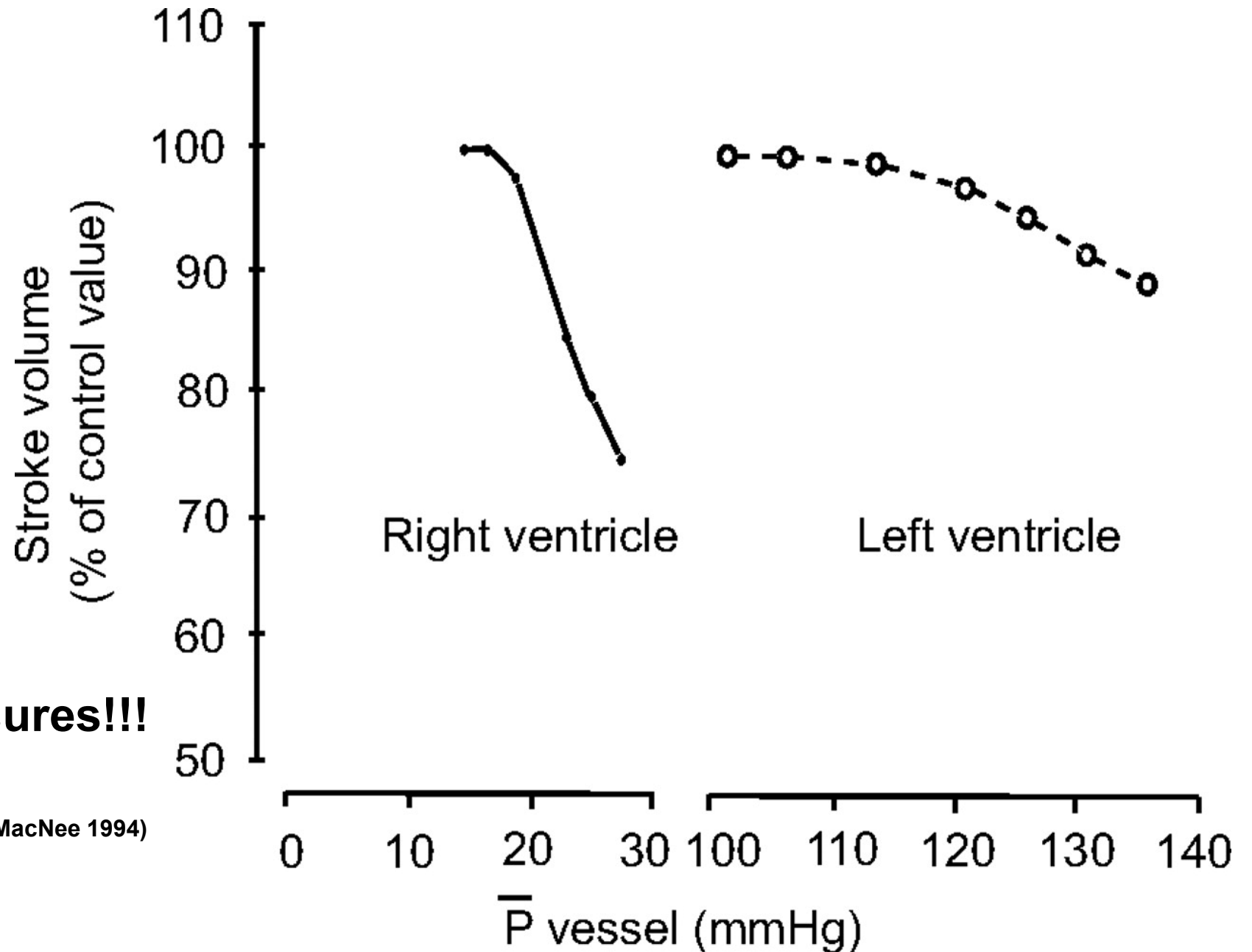
Naser JA et al, JAMA 2025

IMPORTANT: The right ventricle

Thin myocardium (1/3 of LV) is more pliable to accommodate larger variations of venous return. **AND HAS A GREATER SENSITIVITY TO CHANGES IN THE AFTERLOAD**

-> Volume (TR) is better tolerated than increased afterload due to left-sided heart disease

Reduce LV-Filling pressures!!!



François Haddad et al. Circulation. 2008 (Original MacNee 1994)

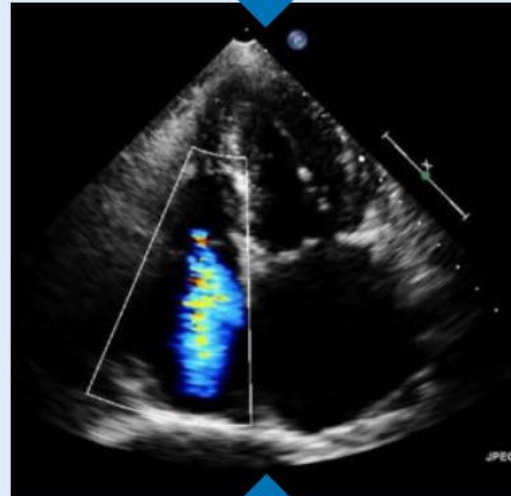
TR: “conservative” treatments must not be forgotten

DIURETICS! Fluid- and salt restriction

Symptomatische/ supportive Therapie

- (Schleifen-)Diuretika
- Flüssigkeits- und Salzrestriktion
- Optimierung von Hämodialyseprotokollen bei terminaler Niereninsuffizienz
- rhythmisierende Therapie bei Vorhofflimmern (z. B. großzügige Indikationsstellung zur Ablation bei Vorhofflattern/-flimmern)
- medikamentöse Bradykardisierung bei Vorliegen einer rechtsventrikulären Insuffizienz vermeiden
- Protonenpumpeninhibitoren bei Stauungsgastritis
- Therapie einer chronisch-venösen Insuffizienz der Beinvenen

Reduktion der
rechtsventrikulären Nachlast
(„Druckentlastung“)



Reduktion der
rechtsventrikulären Vorlast
(„Volumenentlastung“)

Optimal HFrEF treatment (ACE-I, BB, MRA, ARNI, SGLT2-I)

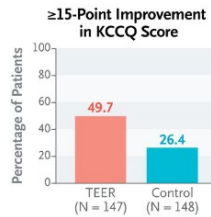
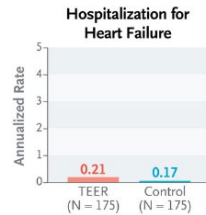
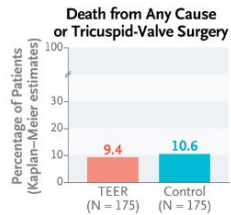
Therapie von Grunderkrankungen

- optimierte Herzinsuffizienztherapie inkl. Gabe von ACE-Hemmern (alternativ Angiotensinrezeptorantagonisten), Betablockern und Mineralokortikoidrezeptorantagonisten, ggf. Angiotensin-Rezeptor-Neprilysin-Inhibitor (ARNI)
- optimale Blutdruckeinstellung **CRT**
- Schlafapnoe-Screening und Therapie
- kardiale Resynchronisationstherapie (CRT) und ggf. kardiale Kontraktilitätsmodulation (CCM)
- chirurgische/interventionelle Korrektur von höhergradigen Aorten-/Mitralklappenvitien
- Einsatz pulmonalerarterieller Vasodilatoren bei (präkapillärer) pulmonalerarterieller Hypertonie
- Thrombolyse bei hämodynamisch relevanter Lungenembolie zur Therapie des Rechtsherzversagens
- antibiotische Therapie einer Trikuspidalklappenendokarditis

Treatments of Atrial fibrillation (z.B. Amiodarone, Ablation...)

Transcatheter Repair for Patients with Tricuspid Regurgitation – TRILUMINATE

	TEER Group (N = 175)	Control Group (N = 175)
Hierarchical composite — no. of wins	11,348	7643



positive "only" due to QOL improvement

Sorajja P et al. NEJM 2023

Tri.fr

T-TEER + OMT vs OMT alone in adult patients with severe, symptomatic tricuspid regurgitation



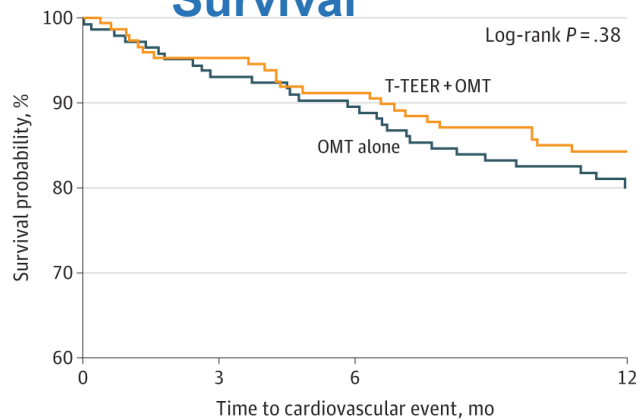
Primary Endpoint (ITT) (1)

At 1-year follow-up, 109 patients (74.1%) in the T-TEER group improved, compared to 58 patients (40.6%) in the GDMT group. The T-TEER group has a probability of a better rank of 0.67; 95% confidence interval, 0.61 to 0.72; P <.0001



ESC Congress 2024 London & Online

Survival

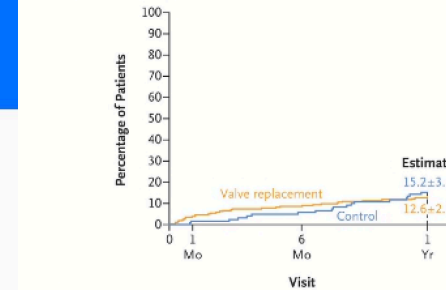


No. at risk	T-TEER + OMT	OMT alone
0	152	147
3	134	128
6	134	128
12	108	85

Donal E et al, JAMA 2025

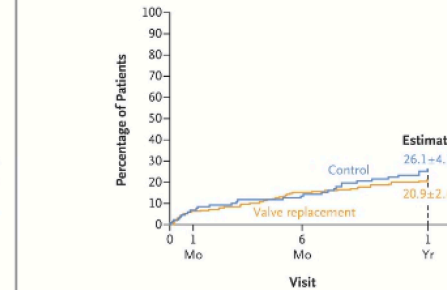
TRISCEND II: Transcatheter Valve Replacement in Severe TR

A Death from Any Cause



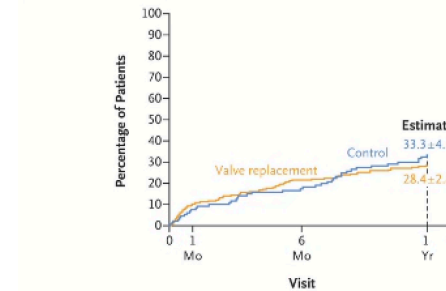
No. at Risk	Valve replacement	Control
0	259	245
1 Mo	245	231
6 Mo	231	216
1 Yr	216	96

B Hospitalization for Heart Failure



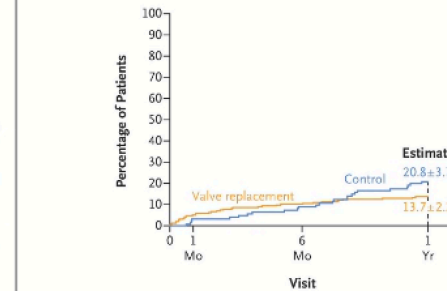
No. at Risk	Valve replacement	Control
0	259	229
1 Mo	229	198
6 Mo	198	176
1 Yr	176	79

C Death from Any Cause or First Hospitalization for Heart Failure



No. at Risk	Valve replacement	Control
0	259	229
1 Mo	229	198
6 Mo	198	176
1 Yr	176	79

D Death from Any Cause or Tricuspid-Valve Intervention



No. at Risk	Valve replacement	Control
0	259	243
1 Mo	243	229
6 Mo	229	215
1 Yr	215	93

Hahn RT et al, NEJM 2025

TR Trials ...

- Open-Label Design. No sham procedure in all these trials – danger of potential placebo effect in patient-reported outcomes (KCCQ) – **difficult to ascertain the true efficacy of the intervention beyond placebo effects.**
- Increased **procedural risks** (e.g. high early mortality and severe bleeding in TRISCEND)
- **No effect on hard clinical endpoints**
- **Selective patient populations**
- **Composite Endpoints that combine subjective measures with objective clinical events complicates interpretation**

Conclusions

- **OMT, together with CRT and coronary revascularization** are the cornerstones for treatment of moderate and severe FMR and FTR
- **Appropriate role of transcatheter interventions for severe FMR and particularly severe FTR is not clear, even after several randomized trials**
- **Carefully selected patients within a heart team approach**



**Thank you for your
attention**

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