



INSTITUT
CARDIOVASCULAIRE
PARIS
SUD

Mitra-FR, Why the trial fails ?

Thierry Lefèvre and the ICPS Team

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Percutaneous Repair or Medical Treatment for Secondary Mitral Regurgitation

J.-F. Obadia, D. Messika-Zeitoun, G. Leurent, B. Lung, 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. Banel, G. Samson, P. Guerin, A. Vahanian, and N. Newton, for the MITRA-FR Investigators*

ESC August 2018

ORIGINAL ARTICLE

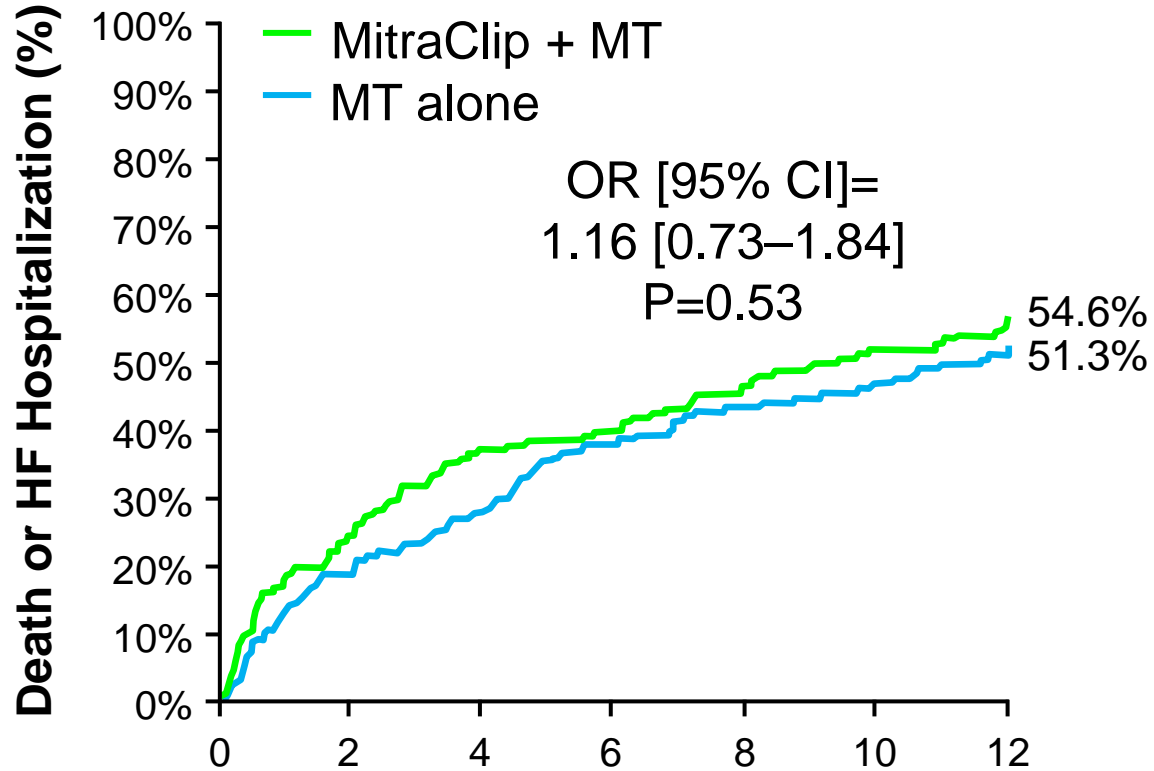
Transcatheter Mitral-Valve Repair in Patients with Heart Failure

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*

TCT September 2018

MITRA-FR vs. COAPT

MITRA-FR

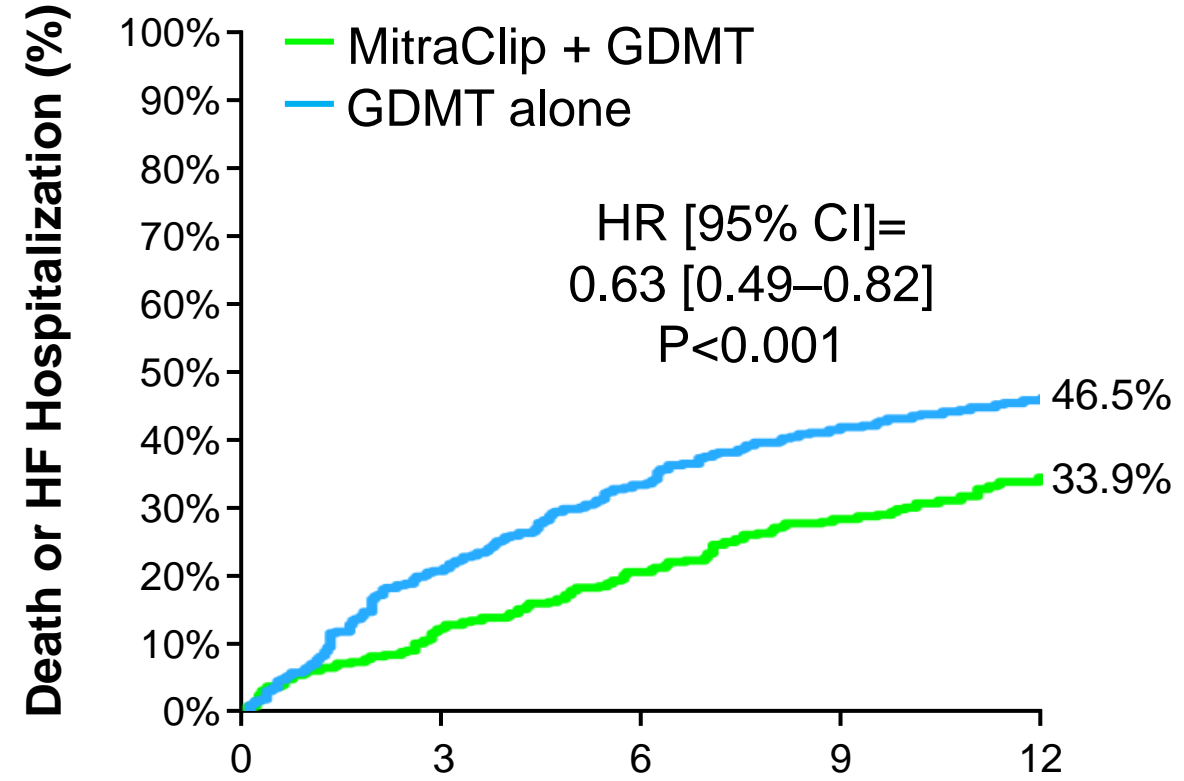


No. at Risk:

Control Group	152	123	109	94	86	80	73
Device Group	151	114	95	91	81	73	67

Obadia JF et al. NEJM. 2018 Aug 27

COAPT

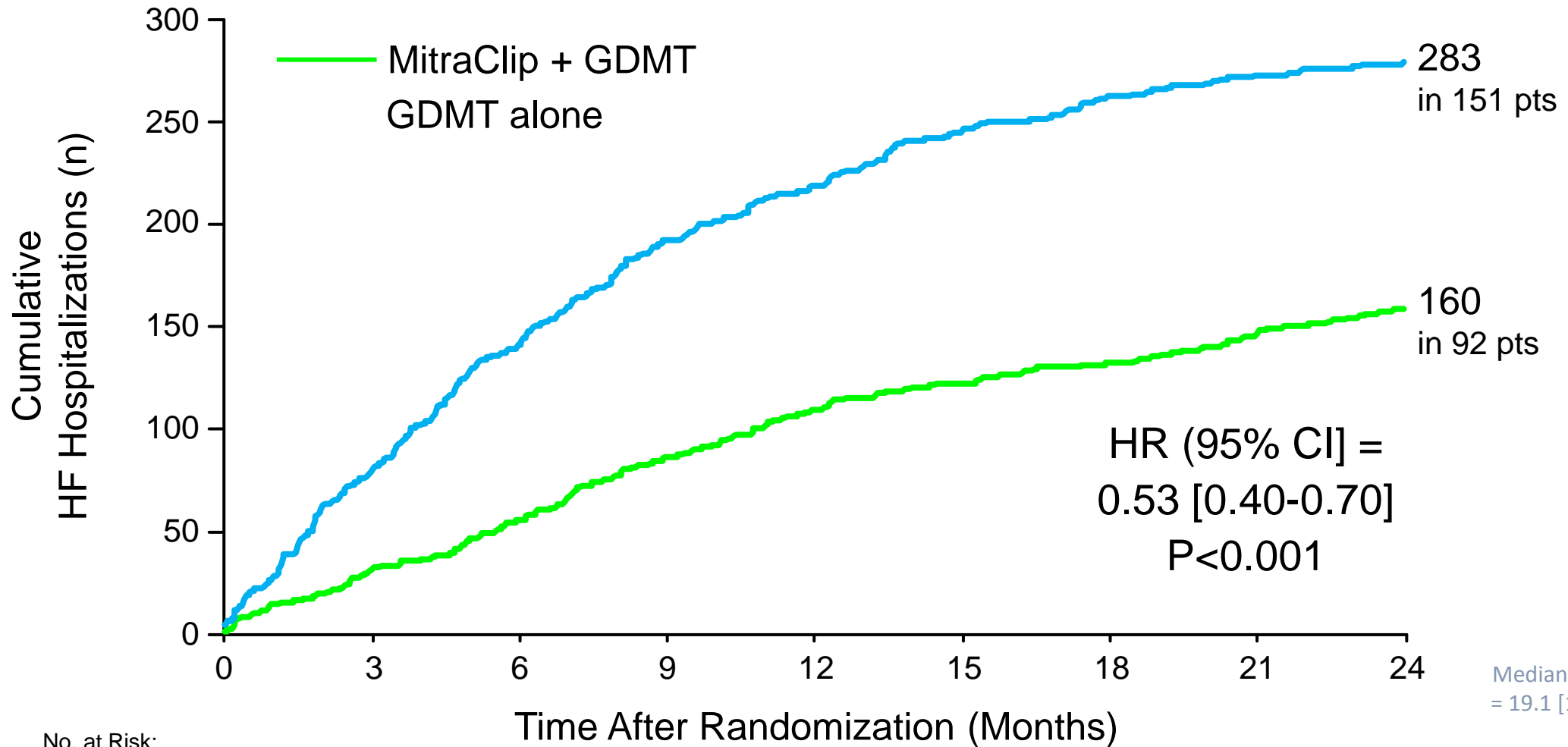


No. at Risk:

Control Group	312	244	205	174	153
Device Group	302	264	238	215	194

Stone GW et al. NEJM. 2018 Sept 23.

Primary Effectiveness Endpoint



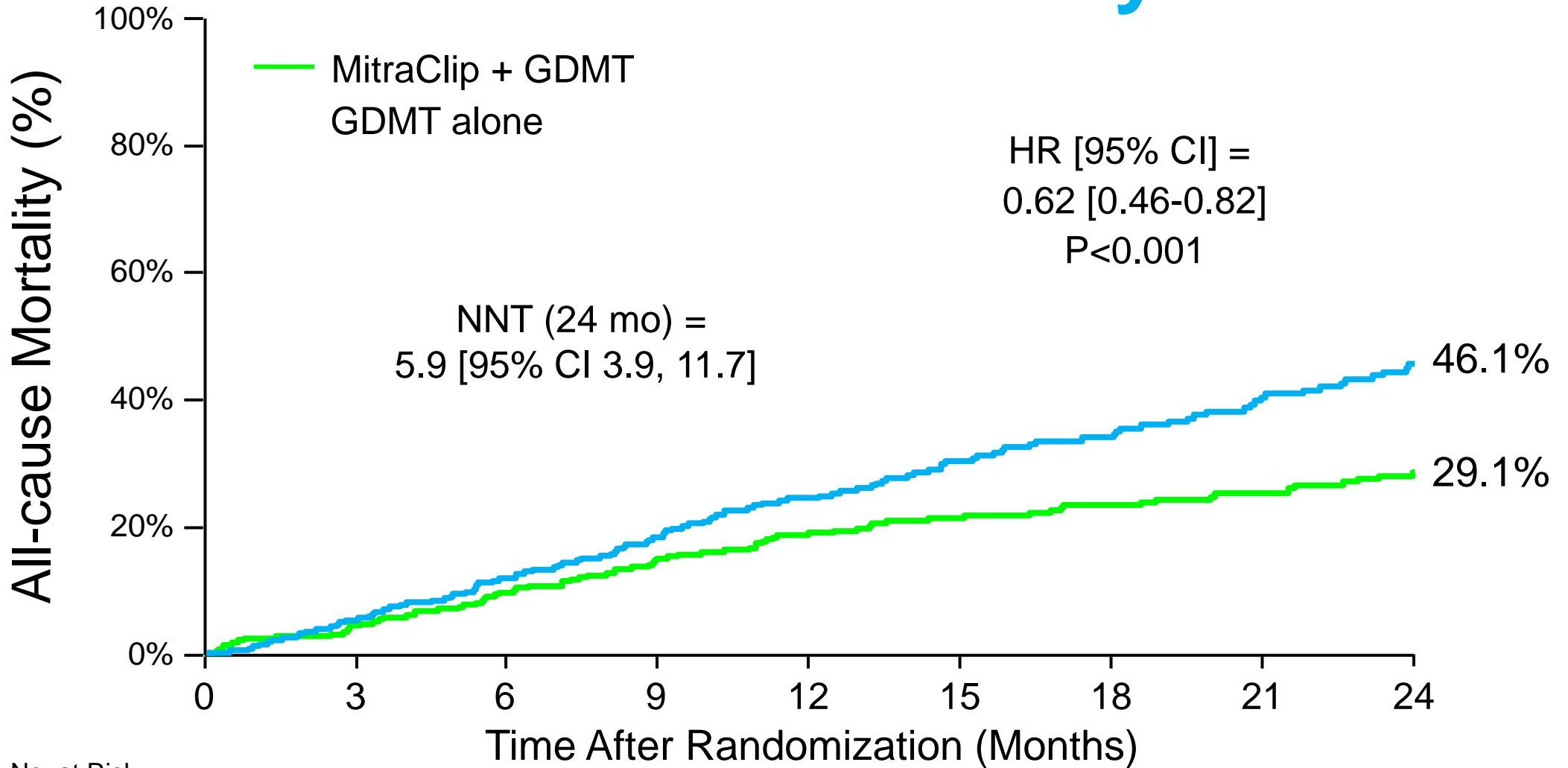
283
in 151 pts

160
in 92 pts

No. at Risk:

MitraClip	302	286	269	253	236	191	178	161	124
GDMT	312	294	271	245	219	176	145	121	88

All-cause Mortality



No. at Risk:

MitraClip + GDMT	302	286	269	253	236	191	178	161	124
GDMT alone	312	294	271	245	219	176	145	121	88

FMR

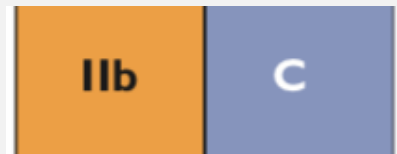


ESC/EACTS GUIDELINES



2017 H Baumgartner et al.

...a percutaneous edge-to-edge procedure may be considered...



ERO > 20 mm²

RV > 30 mL

AHA/ACC Guideline



2017 AHA/ACC Focused Update

...The best therapy for chronic secondary MR is not clear because MR is only 1 component of the disease...

ERO > 40 mm²

RV > 60 mL

MITRA-FR vs. COAPT

Mitra-FR

303 Pts

Primary endpoint 1 year

Academic study

Echocardiographic corelab

EF 15-40%

EROA > 20 mm²

MT per real world practice

No central eligibility committee

Exclusion 32%

Protocol unchanged since 2013

COAPT

614 pts

Primary endpoint 2 year

Industry driven

Echocardiographic corelab

EF 20-50% and LVES diameter \leq 70 ml

EROA \geq 30 mm²

Physician discouraged to change MT

Very selected population

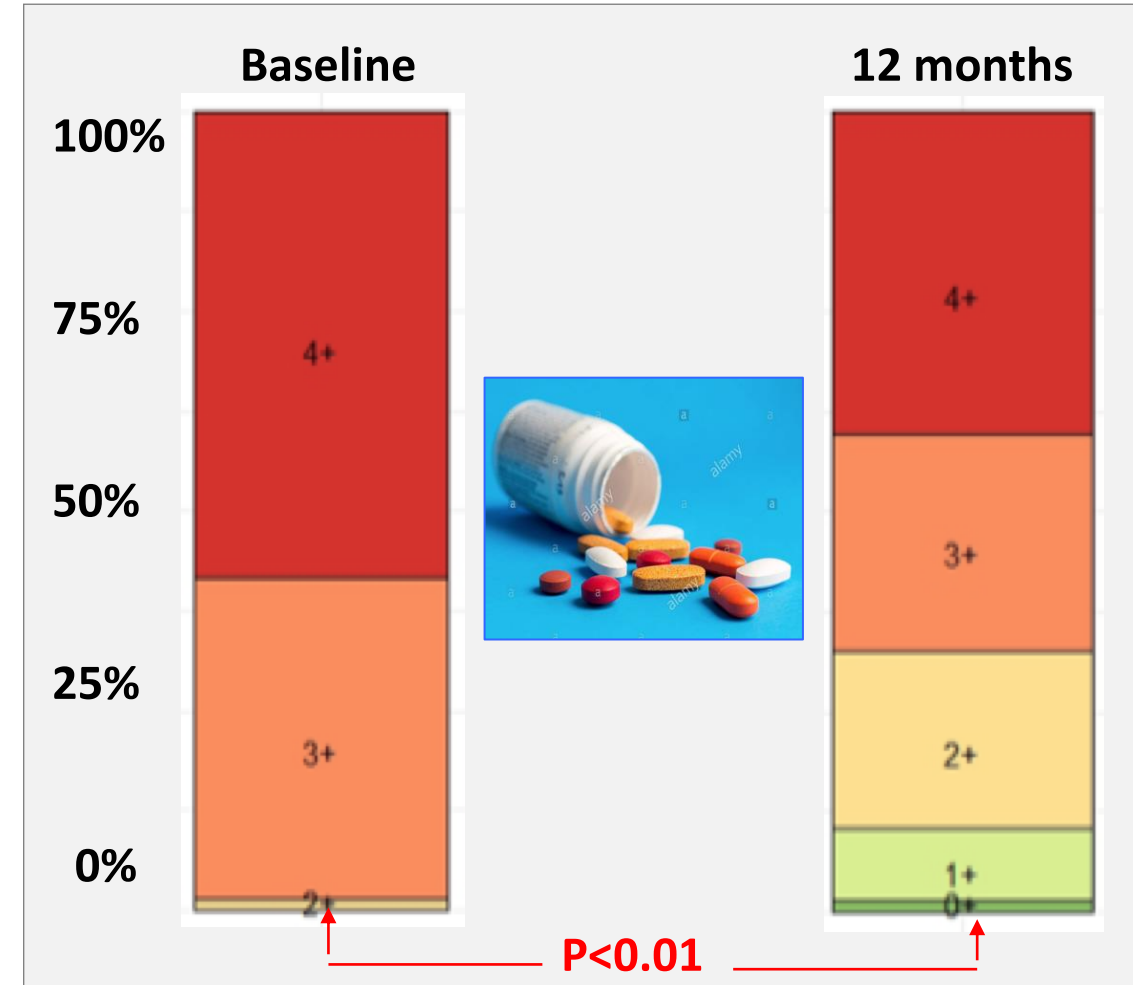
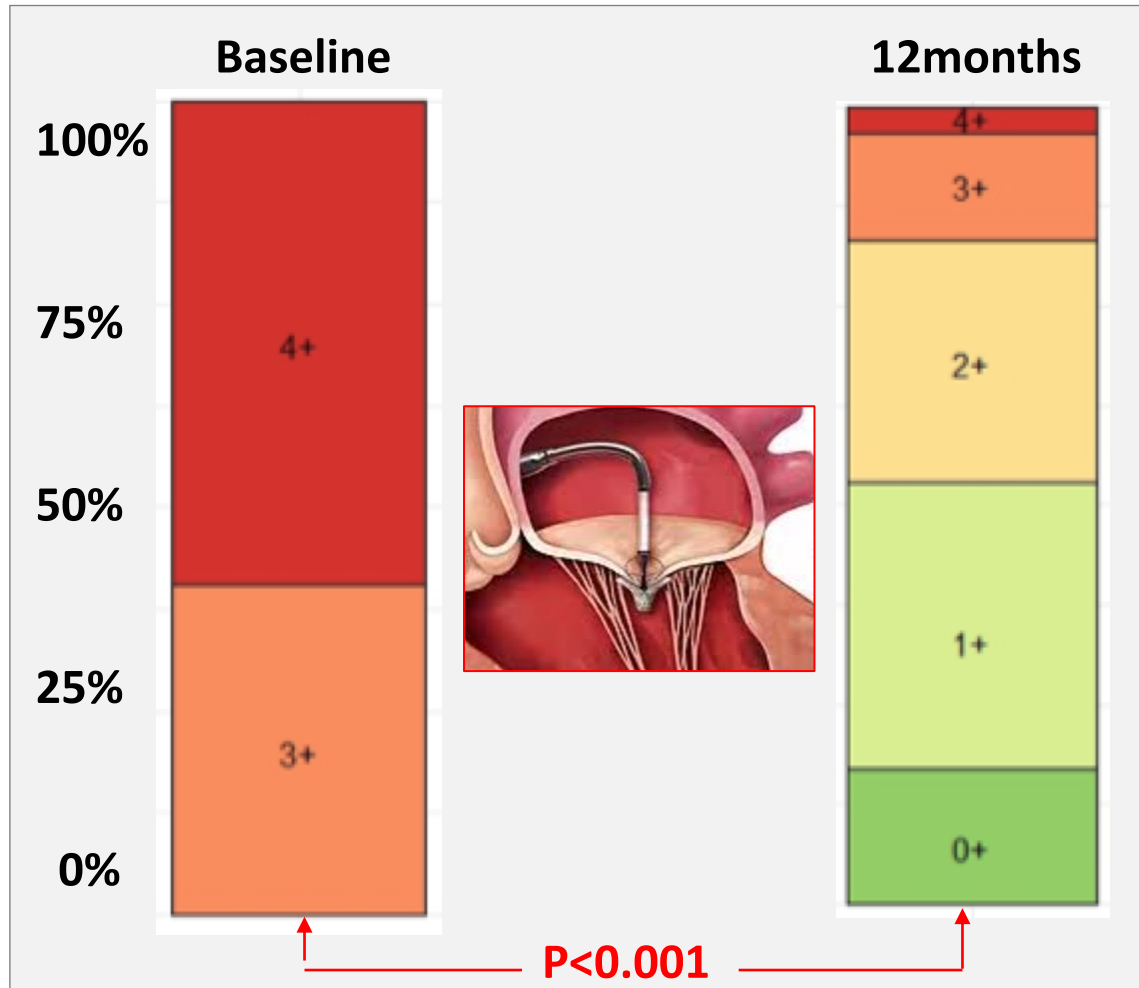
Exclusion 58%

Protocol modified in 2016 (350-610 Pts)

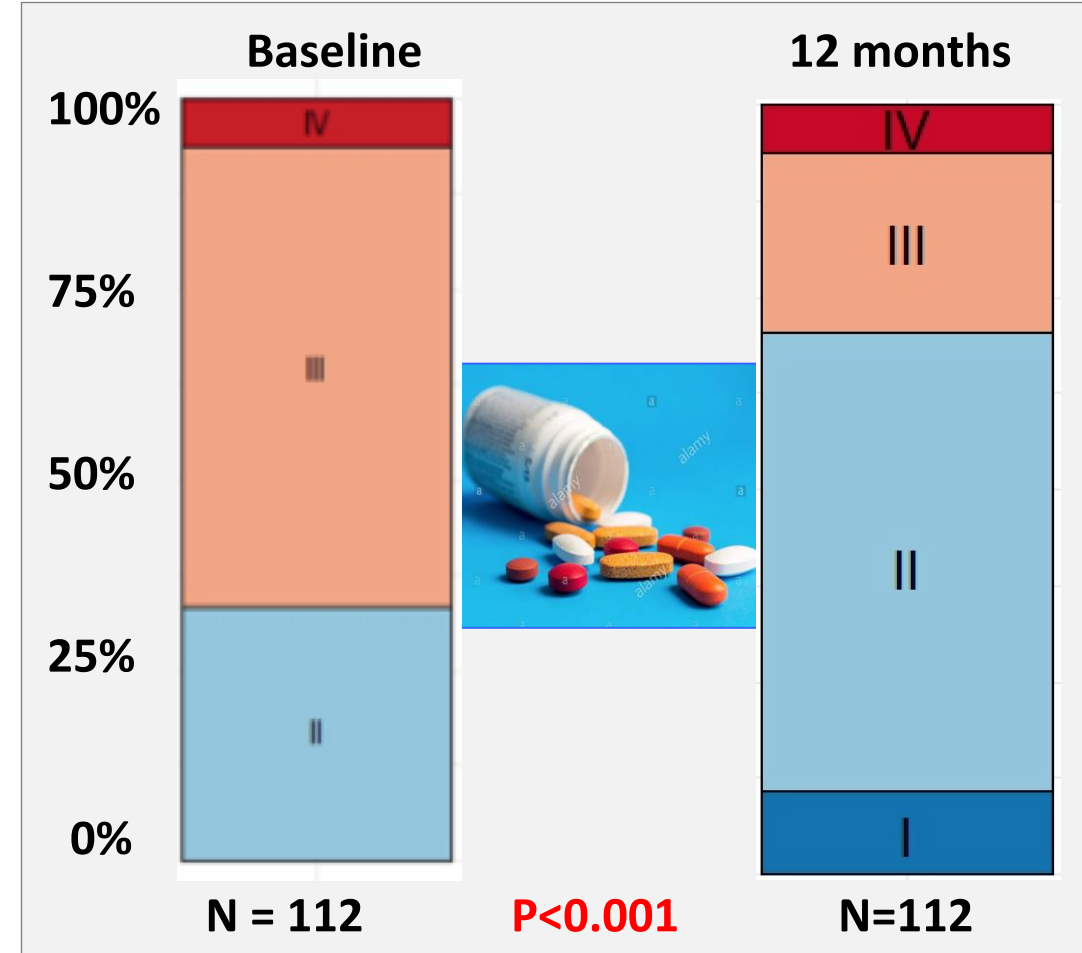
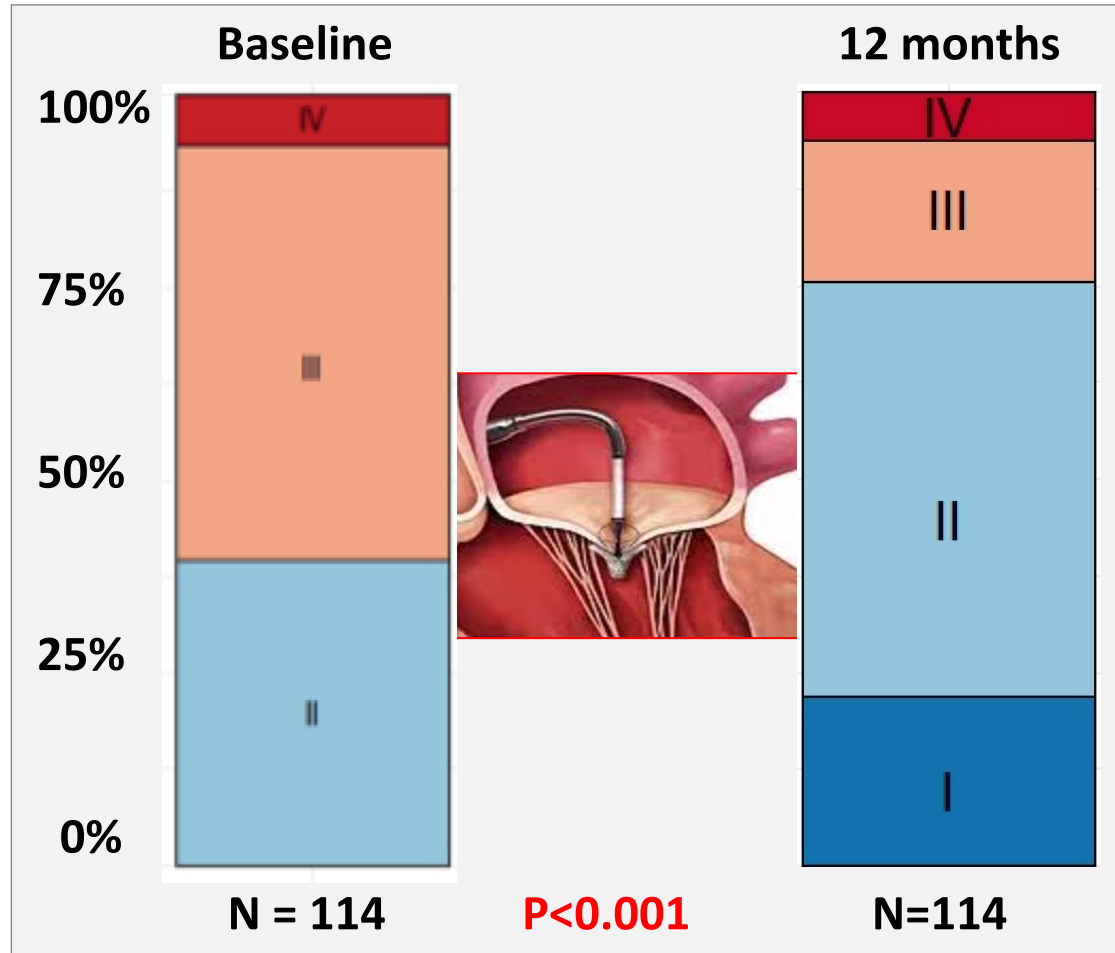
Why this difference between COAPT and Mitra-FR ?

- ✓ 1 year F-up only in Mitra-Fr vs 2 years in COAPT ?
- ✓ Patients really on OMT when included in Mitra-Fr ?
- ✓ Too sick patients in Mitra-Fr ?
- ✓ Entresto approved in France and used during the study ?
- ✓ Learning curve in Mitra-Fr ?
- ✓ The paradigm of disproportionate FMR ?

Evolution of MR in Mitra-FR



Evolution of NYHA class in Mitra-FR



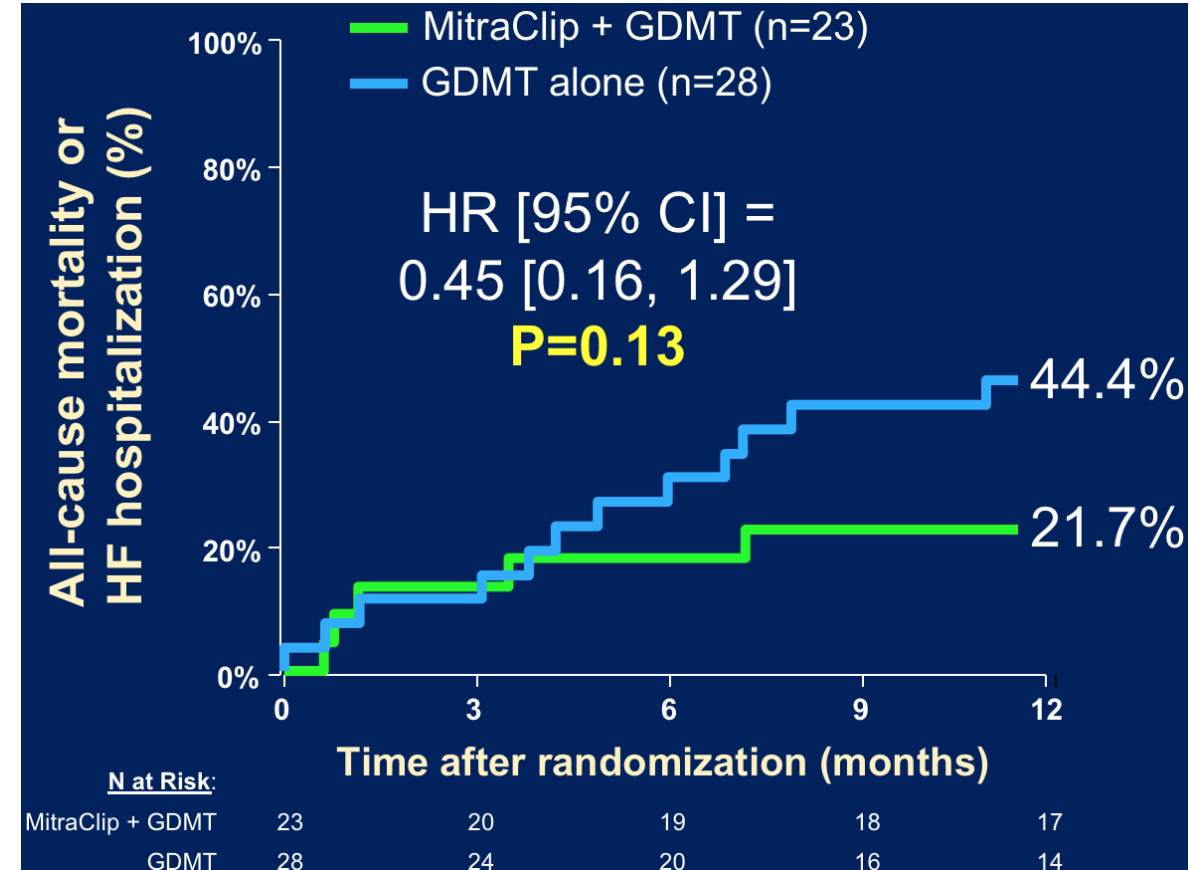
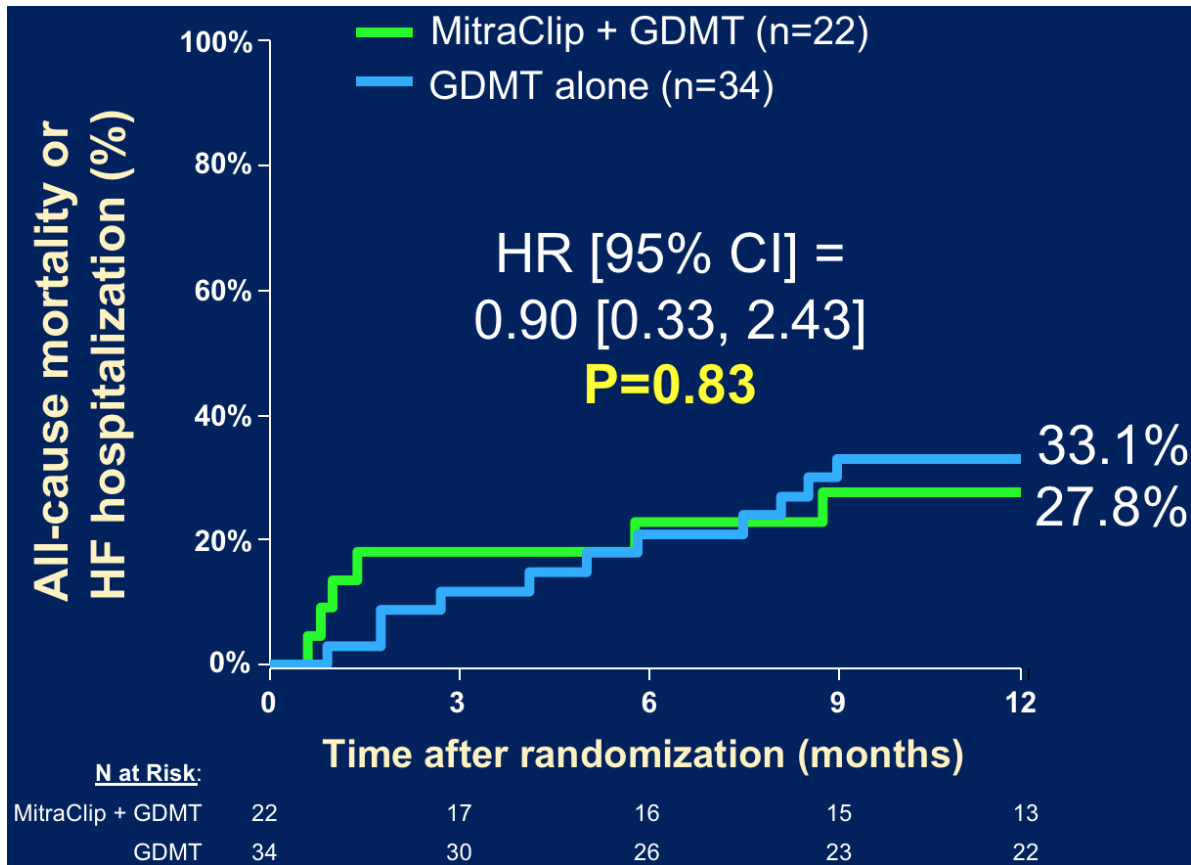
COAPT vs. MITRA-FR: MR, LV Volumes and Function

	COAPT (n=614)	MITRA-FR (n=304)
EROA, mm ² (mean ± SD)	41 ± 15	31 ± 10
- <30 mm ²	14% (80/591)	52% (157/301)
- 30 – 40 mm ²	46% (270/591)	32% (95/301)
- >40 mm ²	41% (241/591)	16% (49/301)
LVEF, % (mean ± SD)	31 ± 9	33 ± 7
LVEDV, mL/m ² (mean ± SD)	101 ± 34	135 ± 35

Impact of EROA and LVEDV: EROA ≤ 30 mm²

LVEDVI >96 ml/m² (N=56; 10.2%)

LVEDVI ≤ 96 ml/m² (N=51; 9.3%)

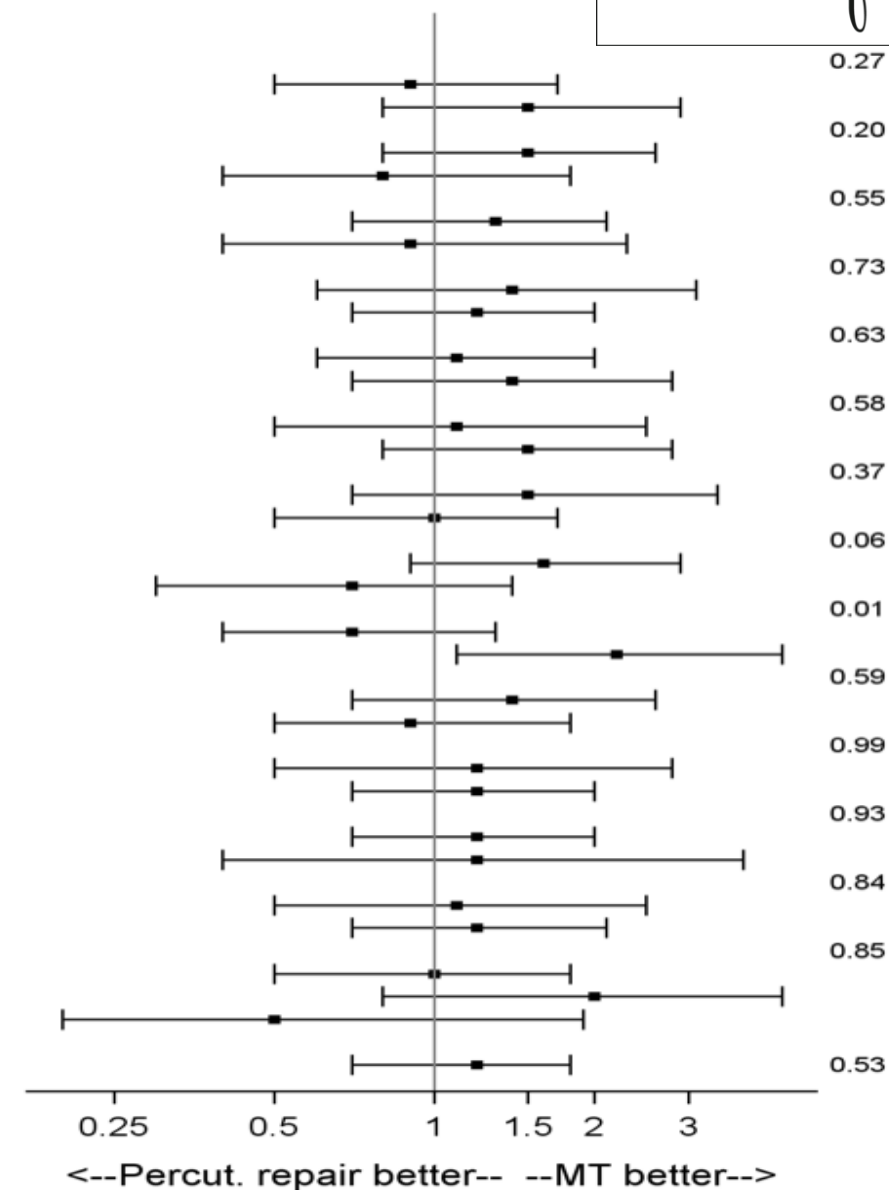


COAPT vs. MITRA-FR: MitraClip Outcomes

	COAPT (n=302)	MITRA-FR (n=152)
MitraClip attempted	293 (97.0%)	144 (94.7%)
≥1 Clip implanted	287 (95.0%)	138 (90.8%)
Device implant failure	6 (2.0%)	6 (4.2%)
Transfusion or vasc compl requiring surgery	16 (5.5%)	5 (3.5%)
Cardiac embolism/stroke	1 (0.3%)	2 (1.4%)
Tamponade	1 (0.3%)	2 (1.5%)
Urgent cardiac surgery	1 (0.3%)	0 (0%)
Acute result: MR ≥3+	5%	9%
12-month result: MR ≥3+	5%	17%



Subgroup	Percut. repair Events/N (%)		Medical treatment Events/N (%)		OR (95% CI)
CENTRE SIZE					
N <= 15 Randomized patients	33/73	(45.2)	35/73	(47.9)	0.90 (0.50, 1.70)
N > 15 Randomized patients	50/77	(64.9)	43/78	(55.1)	1.50 (0.80, 2.90)
AGE					
<= 75 Yr	52/100	(52.0)	39/93	(41.9)	1.50 (0.80, 2.60)
> 75 Yr	31/50	(62.0)	39/58	(67.2)	0.80 (0.40, 1.80)
GENDER					
Male	67/120	(55.8)	53/106	(50.0)	1.30 (0.70, 2.10)
Female	16/30	(53.3)	25/45	(55.6)	0.90 (0.40, 2.30)
NYHA					
Class II	26/56	(46.4)	17/44	(38.6)	1.40 (0.60, 3.10)
Class III/IV	57/94	(60.6)	61/107	(57.0)	1.20 (0.70, 2.00)
ISCHEMIC CARDIOMYOPATHY					
Yes	49/94	(52.1)	42/84	(50.0)	1.10 (0.60, 2.00)
No	34/56	(60.7)	35/66	(53.0)	1.40 (0.70, 2.80)
PULMONARY ARTERY PRESSURE					
< 50 mmHg	23/53	(43.4)	18/44	(40.9)	1.10 (0.50, 2.50)
≥ 50 mmHg	49/73	(67.1)	51/88	(58.0)	1.50 (0.80, 2.80)
ATRIAL FIBRILLATION					
Yes	30/49	(61.2)	24/47	(51.1)	1.50 (0.70, 3.40)
No	46/91	(50.5)	51/99	(51.5)	1.00 (0.50, 1.70)
PREVIOUS HOSPIT FOR CHF					
< 2	53/95	(55.8)	38/87	(43.7)	1.60 (0.90, 2.90)
≥ 2	30/55	(54.5)	40/62	(64.5)	0.70 (0.30, 1.40)
CREATININE					
< 1.5 mg/dl	31/75	(41.3)	43/85	(50.6)	0.70 (0.40, 1.30)
≥ 1.5 mg/dl	51/72	(70.8)	34/65	(52.3)	2.20 (1.10, 4.50)
HEMOGLOBINE					
< Median	43/75	(57.3)	33/65	(50.8)	1.40 (0.70, 2.60)
≥ Median	38/72	(52.8)	42/80	(52.5)	0.90 (0.50, 1.80)
LVEF					
< 30%	21/35	(60.0)	27/48	(56.3)	1.20 (0.50, 2.80)
≥ 30%	62/115	(53.9)	51/102	(50.0)	1.20 (0.70, 2.00)
TRICUSPID REGURGITATION					
Mild	60/110	(54.5)	60/118	(50.8)	1.20 (0.70, 2.00)
Moderate/Severe	19/29	(65.5)	14/23	(60.9)	1.20 (0.40, 3.80)
LV TELEDIASTOLIC DIAMETER					
< 65 mm	21/43	(48.8)	21/45	(46.7)	1.10 (0.50, 2.50)
≥ 65 mm	62/107	(57.9)	56/105	(53.3)	1.20 (0.70, 2.10)
MITRAL REGURGITANT ORIFICE					
< 30 mm ²	37/77	(48.1)	39/80	(48.8)	1.00 (0.50, 1.80)
30-40 mm ²	28/44	(63.6)	24/51	(47.1)	2.00 (0.80, 4.50)
> 40 mm ²	18/29	(62.1)	15/20	(75.0)	0.50 (0.20, 1.90)
OVERALL	83/150	(55.3)	78/151	(51.7)	1.20 (0.70, 1.80)

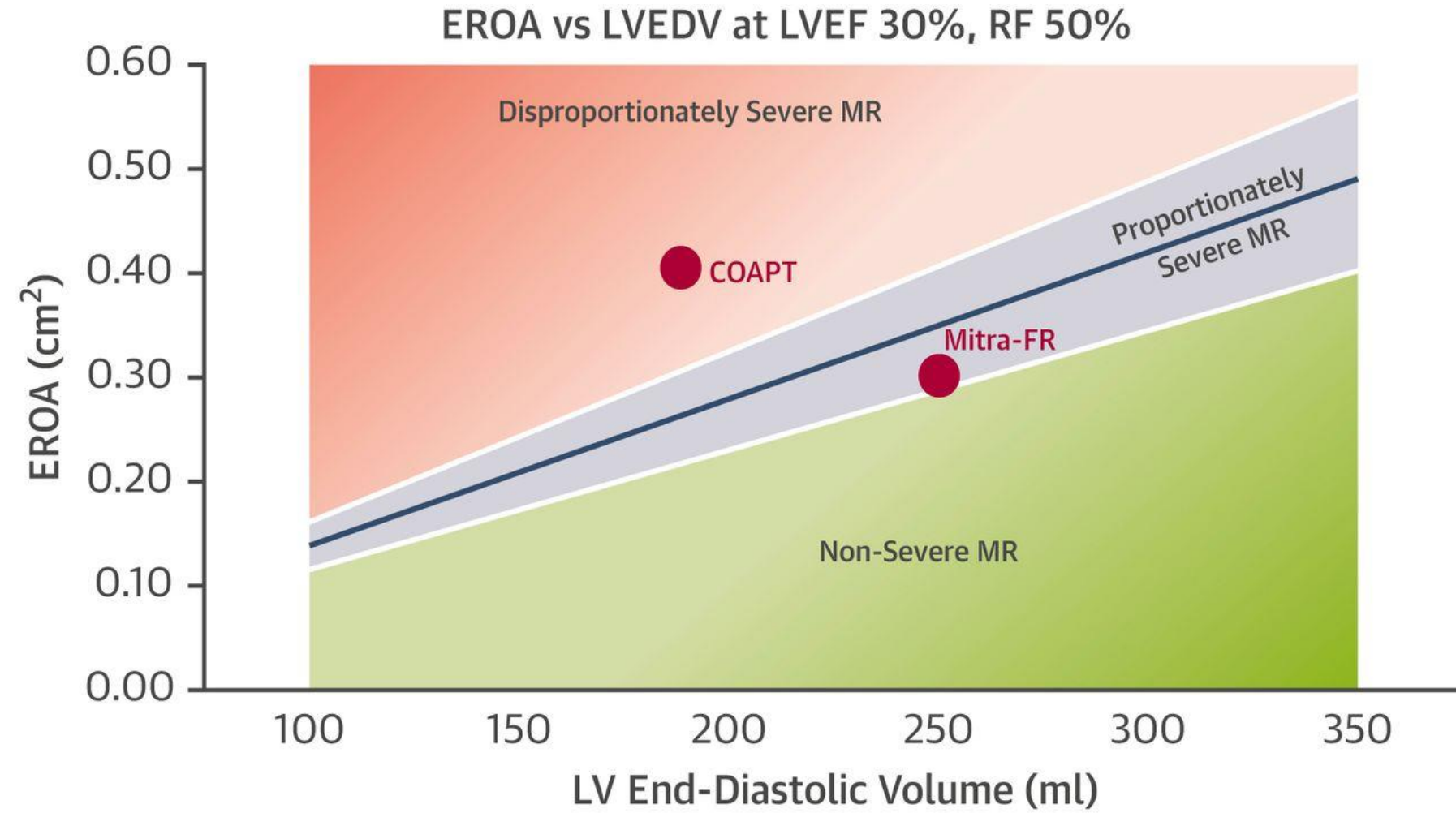



EDITORIAL VIEWPOINT

Proportionate and Disproportionate Functional Mitral Regurgitation

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

Proportionate or disproportionate FMR ?



Conclusion

MITRA-FR, that represented more of a real-life population with its wide inclusion criteria for MitraClip therapy, led to disappointing results at 1 year.

COAPT focused on very selected patients with smaller ventricles, better RV function and more disproportionate MR in whom the correction of MR saves lives and limits the rehospitalisation rate.

The definition of severe MR should be revisited regarding the ventricular parameter before treating FMR patients with Mitraclip.