How to Identify the RIGHT (and WRONG) Patient for Transcatheter Mitral Repair

Anita W. Asgar MD, MSc, FRCPC, FACC

Professeur aggregé, université de Montreal

Institut de Cardiologie de Montreal

Disclosures

- Abbott Structural: Consulting, Honoraria, Research Support
- Medtronic: Consulting, Proctor, Honoraria
- Edwards: Consulting, Honoraria

Objectives

- Understand the diagnostic pathway for determining patient eligibility for percutaneous mitral interventions
- Discuss discrepant results that have been reported in recent mitral intervention studies
- Review the routine follow-up of patients post-mitral clip procedures

Case Presentation

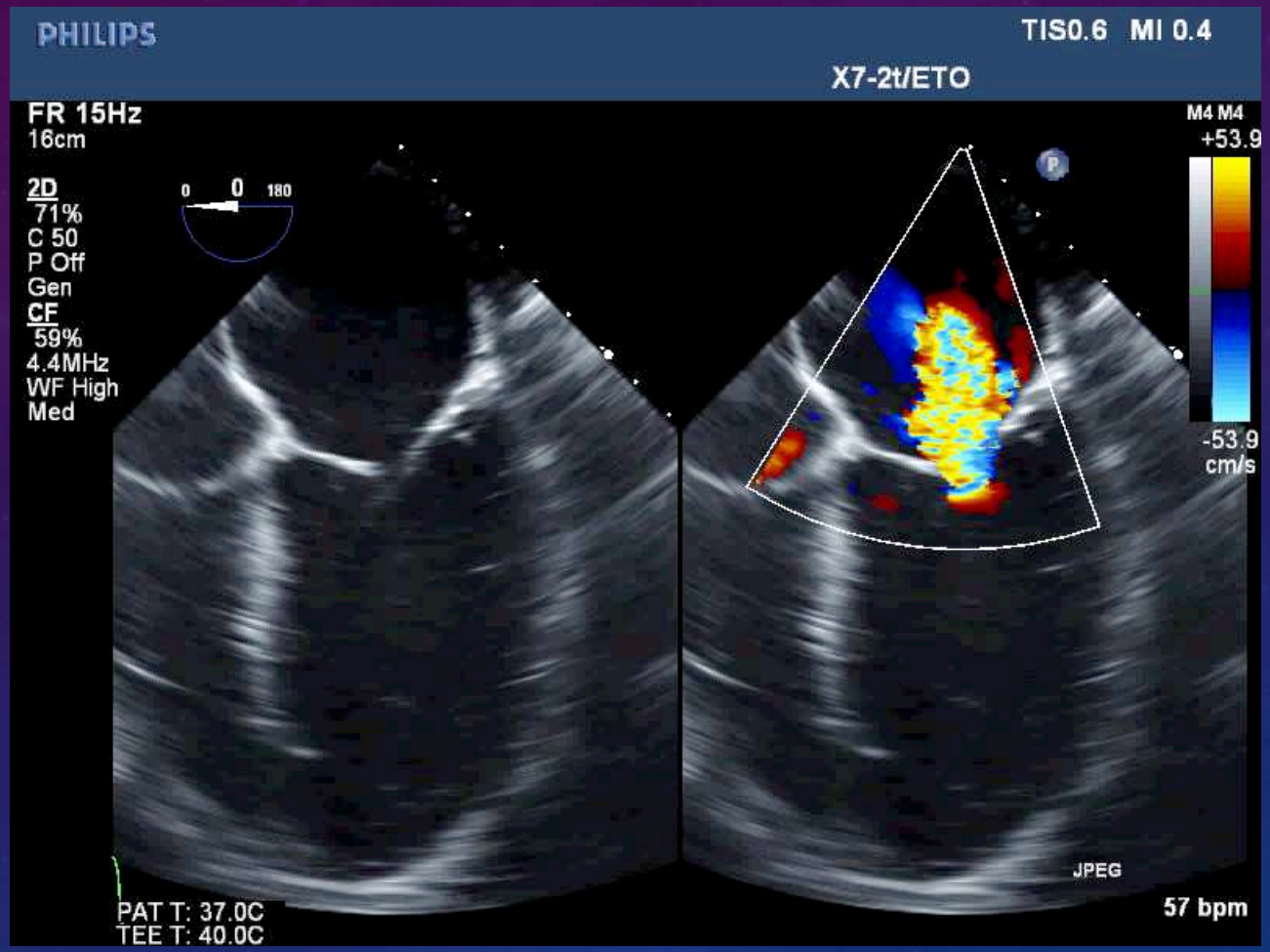
- 72 year old male followed in the Heart Failure Clinic with ischemic cardiomyopathy, NYHA Class III
- Previous History
  - IHD: Previous PCI LAD and Cx
  - Hypertension
  - Diabetes
  - Dyslipidemia
  - Chronic Atrial Flutter- on Coumadin
  - Anemia
  - CRF: creat 306
  - COPD

CASE PRESENTATION

- Medical therapy:
  - Lasix 80mg BID
  - Zaroxylyn 2.5 mg die
  - Bisoprolol 7.5mg
  - Aldactone 25 mg die
  - Imdur 60 mg die
  - Hydralazine 25 mg TID
  - Eprex
  - Crestor 10 mg die
  - Insulin

- Echocardiogram:
  - LVEF 33%
  - LV 64/50
  - PAP 46mmHg
  - MR 4/4
  - TR 1/4
  - Normal RV function

Case Presentation



Is this a reasonable patient for transcatheter mitral repair?

Question #1

What is NOT an important factor to consider when selecting a patient for transcatheter mitral repair (MitraClip)?

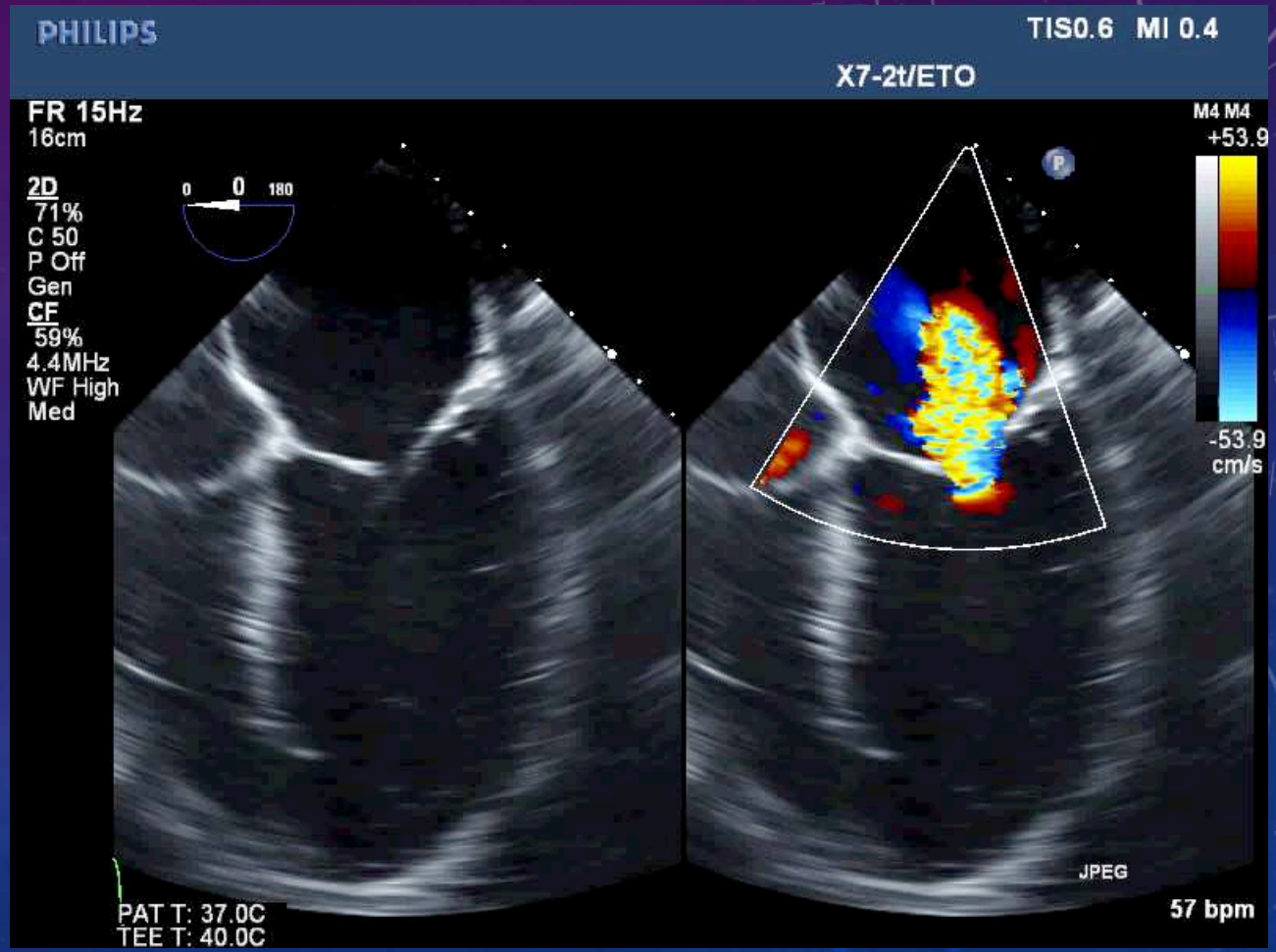
A. Ejection Fraction
B. Severity of Mitral regurgitation
C. Etiology of cardiomyopathy
D. Current medical therapy
E. Severity of Pulmonary Hypertension
F. Severity of TR

Evaluation of a Patient for MitraClip

- Clinical evaluation
  - Is the patient symptomatic?
  - Is there a reasonable chance that treating FMR will improve quality of life? Are the comorbidities prohibitive?
- Transthoracic Echo
  - Severity of MR, LV Function, Coexistent valvular heart disease
  - RV function
- Transesophageal Echo
  - Mechanism of MR
  - Mitral valve area

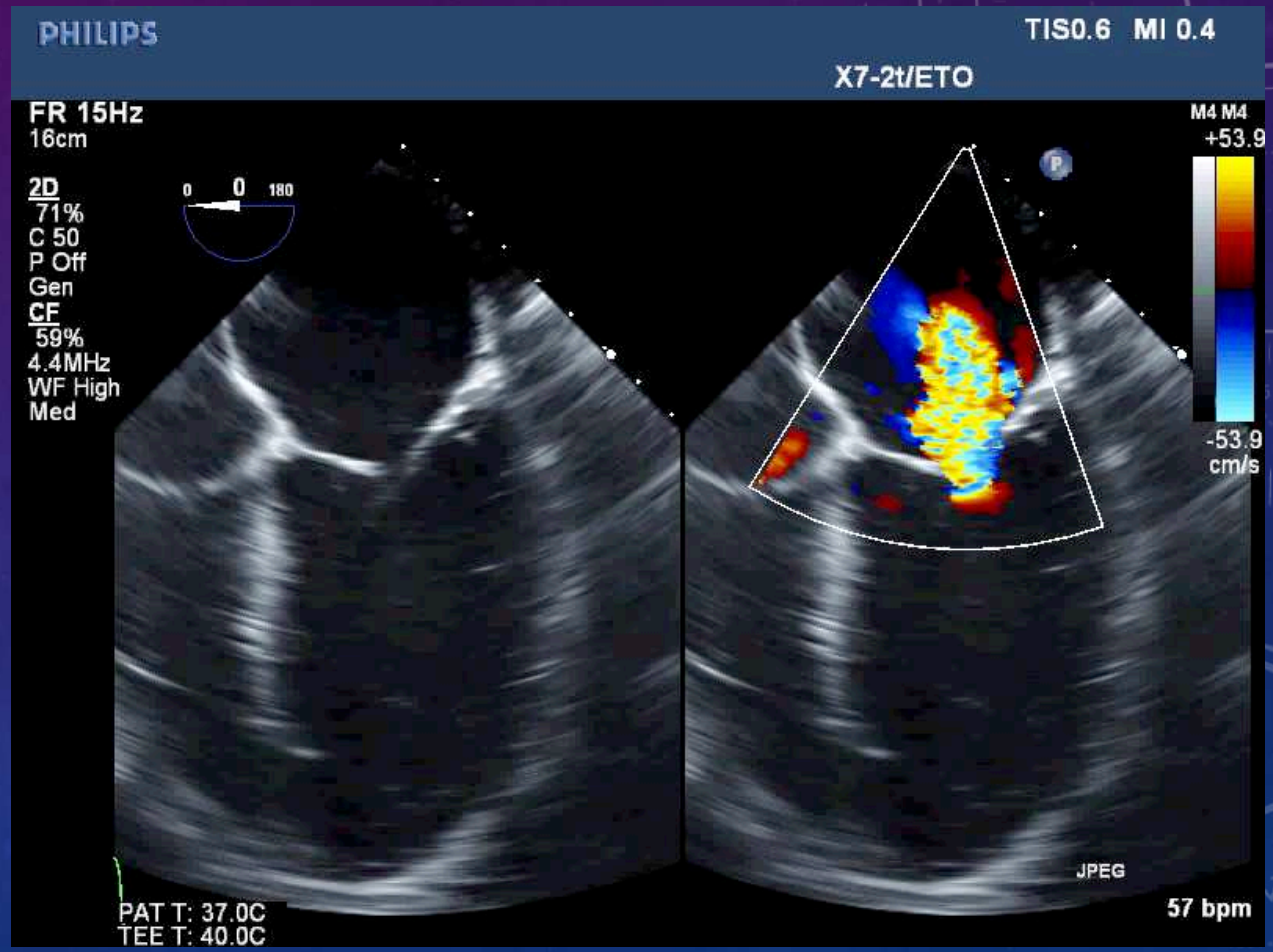
Case Presentation

- Patient discussed at Heart Team meeting decision made to propose COAPT Trial
- Patient consented for participation in the COAPT Trial (12/2016) and randomized to medical therapy



Case Presentation

- Twelve months following randomization to ***Medical Therapy in COAPT***:
  - Hospitalized for decompensated heart failure on **18** separate occasions (January 2017-December 2017)
  - Renal function deteriorating, creat 400
  - NYHA IV



Secondary Mitral Regurgitation

ORIGINAL ARTICLE

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*

ABSTRACT

BACKGROUND
In patients who have chronic heart failure with reduced left ventricular ejection fraction, severe secondary mitral-valve regurgitation is associated with a poor prognosis. Whether percutaneous mitral-valve repair improves clinical outcomes in this patient population is unknown.

METHODS
We randomly assigned patients who had severe secondary mitral regurgitation (defined as an effective regurgitant orifice area of ≥20 mm² or a regurgitant volume of ≥30 ml per beat), a left ventricular ejection fraction between 15 and 40%, and symptomatic heart failure, in a 1:1 ratio, to undergo percutaneous mitral-valve repair in addition to receiving medical therapy (intervention group; 152 patients) or to receive medical therapy alone (control group; 152 patients). The primary efficacy outcome was a composite of death from any cause or unplanned hospitalization for heart failure at 12 months.

RESULTS
At 12 months, the rate of the primary outcome was 54.6% (83 of 152 patients) in the intervention group and 51.3% (78 of 152 patients) in the control group (odds ratio, 1.16; 95% confidence interval [CI], 0.73 to 1.84; P=0.53). The rate of death from any cause was 24.3% (37 of 152 patients) in the intervention group and 22.4% (34 of 152 patients) in the control group (hazard ratio, 1.11; 95% CI, 0.69 to 1.77). The rate of unplanned hospitalization for heart failure was 48.7% (74 of 152 patients) in the intervention group and 47.4% (72 of 152 patients) in the control group (hazard ratio, 1.13; 95% CI, 0.81 to 1.56).

CONCLUSIONS
Among patients with severe secondary mitral regurgitation, the rate of death or unplanned hospitalization for heart failure at 1 year did not differ significantly between patients who underwent percutaneous mitral-valve repair in addition to receiving medical therapy and those who received medical therapy alone. (Funded by the French Ministry of Health and Research National Program and Abbott Vascular; MITRA-FR ClinicalTrials.gov number, NCT01920698.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Obadia at Hôpital Cardiovasculaire Louis Pradel, Chirurgie Cardio-Vasculaire et Transplantation Cardiaque, 28, Ave. Doyen Lépine, 69677 Bron CEDEX, France, or at jean-francois.obadia@chu-lyon.fr.

*A list of investigators in the MITRA-FR trial is provided in the Supplementary Appendix, available at NEJM.org.

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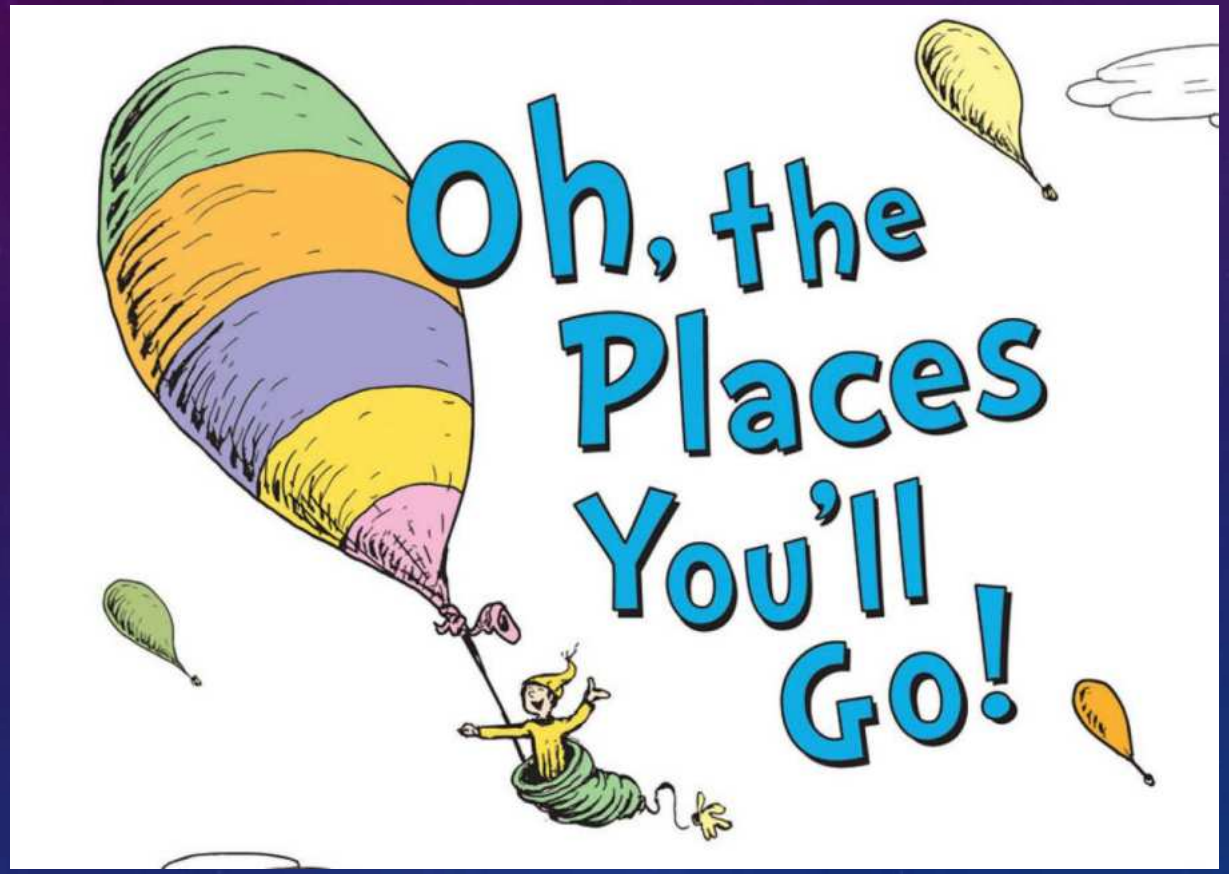
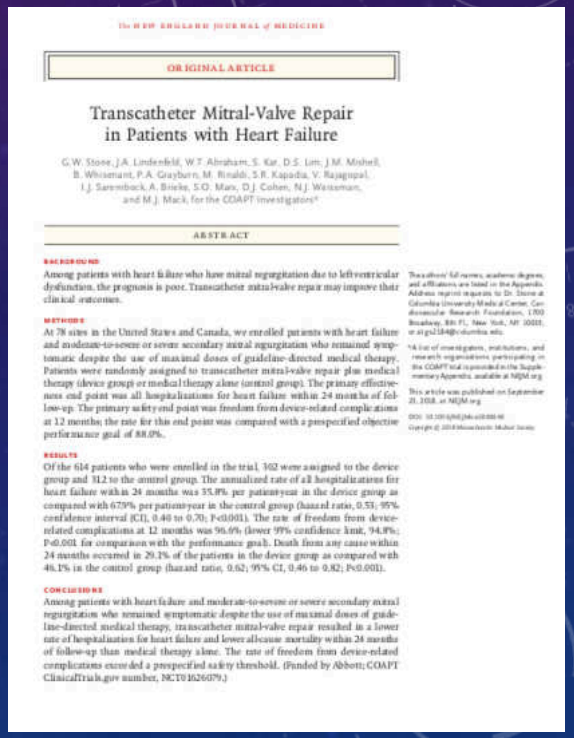
MITRA-FR
August 2018



Theodor Seuss "Ted" Geisel (1904-1991)



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*

ABSTRACT

BACKGROUND
Among patients with heart failure who have mitral regurgitation due to left ventricular dysfunction, the prognosis is poor. Transcatheter mitral-valve repair may improve their clinical outcomes.

METHODS
At 78 sites in the United States and Canada, we enrolled patients with heart failure and moderate-to-severe or severe secondary mitral regurgitation who remained symptomatic despite the use of maximal doses of guideline-directed medical therapy. Patients were randomly assigned to transcatheter mitral-valve repair plus medical therapy (device group) or medical therapy alone (control group). The primary effectiveness end point was all hospitalizations for heart failure within 24 months of follow-up. The primary safety end point was freedom from device-related complications at 12 months; the rate for this end point was compared with a prespecified objective performance goal of 88.0%.

RESULTS
Of the 614 patients who were enrolled in the trial, 302 were assigned to the device group and 312 to the control group. The annualized rate of all hospitalizations for heart failure within 24 months was 35.8% per patient-year in the device group as compared with 67.9% per patient-year in the control group (hazard ratio, 0.53; 95% confidence interval [CI], 0.40 to 0.70; P<0.001). The rate of freedom from device-related complications at 12 months was 96.6% (lower 95% confidence limit, 94.8%; P<0.001 for comparison with the performance goal). Death from any cause within 24 months occurred in 29.1% of the patients in the device group as compared with 46.1% in the control group (hazard ratio, 0.62; 95% CI, 0.46 to 0.82; P=0.001).

CONCLUSIONS
Among patients with heart failure and moderate-to-severe or severe secondary mitral regurgitation who remained symptomatic despite the use of maximal doses of guideline-directed medical therapy, transcatheter mitral-valve repair resulted in a lower rate of hospitalization for heart failure and lower all-cause mortality within 24 months of follow-up than medical therapy alone. The rate of freedom from device-related complications exceeded a prespecified safety threshold. (Funded by Abbott; COAPT ClinicalTrials.gov number, NCT01626079.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Stone at Columbia University Medical Center, Cardiovascular Research Foundation, 1700 Broadway, 8th Fl., New York, NY 10019, or at gs2184@cumc.edu.

*A list of investigators, institutions, and research organizations participating in the COAPT trial is provided in the Supplementary Appendix, available at NEJM.org.

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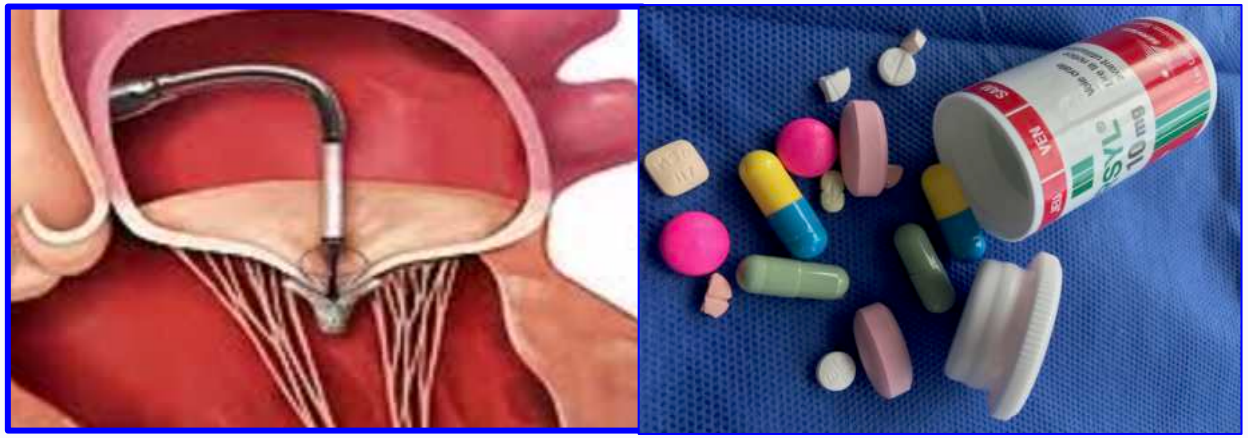
COAPT
September 2018

Question #2

What does the evidence from MITRA-FR and COAPT suggest about the utility of MitraClip in secondary MR?

A. There is no benefit of MitraClip in secondary MR
B. Treatment with MitraClip reduces HF hospitalizations in ALL patients with secondary MR
C. Treatment with MitraClip reduces all cause mortality in ALL patients with secondary MR
D. There is benefit of MitraClip in selected patients with secondary MR
E. Proportionately severe MR is a characteristic of those who benefit from MitraClip

Percutaneous Repair with the MitraClip Device for Severe Secondary Mitral Regurgitation



Pr Jean François OBADIA - LYON

on behalf of the MITRA-FR Investigators

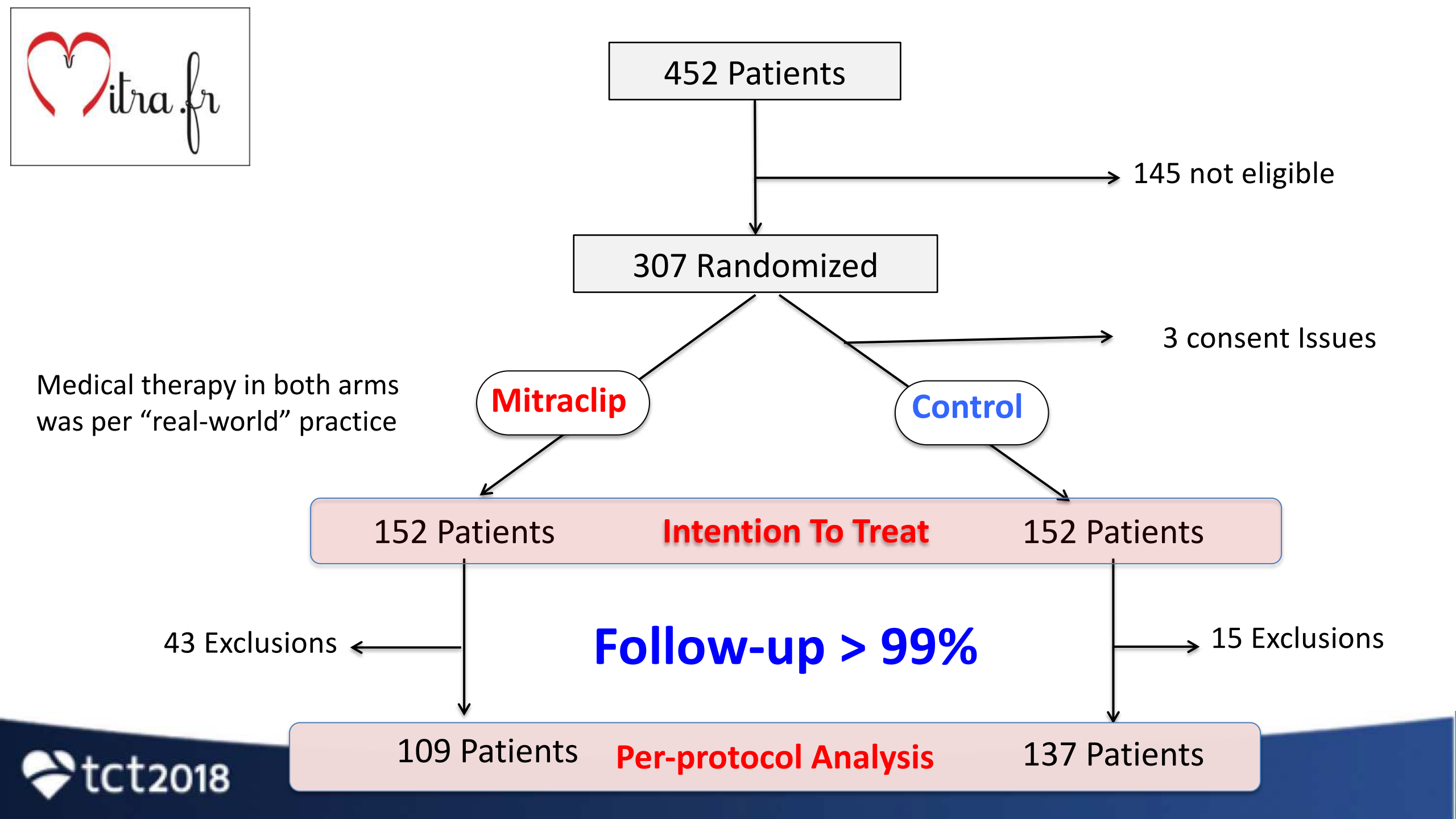
Academic Study*

Primary Endpoint "Composite" All-Cause Deaths or Unplanned rehospitalisation for Heart failure at 12 months

** Obadia et al. Eurointervention 2015;10:1354-1360*

Inclusion Criteria

- Symptomatic despite Optimal Treatment (NYHA ≥II).
- At least one hospitalization for HF within 12 months preceding randomization
- Severe Secondary MR → ERO > 20 mm^2 or R.vol>30 mL/beat
- 15% < EF < 40%
- Not eligible for surgery "Heart Team"
- Centralized echocardiographic Corelab


Mitra.fr
452 Patients
145 not eligible
307 Randomized
3 consent Issues
Medical therapy in both arms was per "real-world" practice
Mitraclip
Control
152 Patients
Intention To Treat
152 Patients
43 Exclusions
Follow-up > 99%
15 Exclusions
109 Patients
Per-protocol Analysis
137 Patients
tct2018

Baseline characteristics

Characteristics	Percutaneous Repair Group (n=152)	Optimal Medical Treatment Group (n=152)	P value
Age year mean (±SD)	70.1 ± 10.1	70.6 ± 9.9	0.69
>75 year n (%)	51 (33.6)	59 (38.8%)	0.40
Males n - (%)	120 (78.9)	107 (70.4%)	0.11
Ischemic Cardiomyopathy n - (%)	95 (62.5)	85 (56.3%)	0.29
NYHA Class II n - (%)	56 (36.8)	44 (28.9%)	
NYHA Class III n - (%)	82 (53.9)	96 (63.2%)	0.27
NYHA Class IV n - (%)	14 (9.2)	12 (7.9%)	
LVEF mean (±SD)	33.3 ± 6.5	32.9 ± 6.7	0.79
Effect regurg. Orif. area - mm^2 mean (±SD)	31 ± 10	31 ± 11	0.42

60%

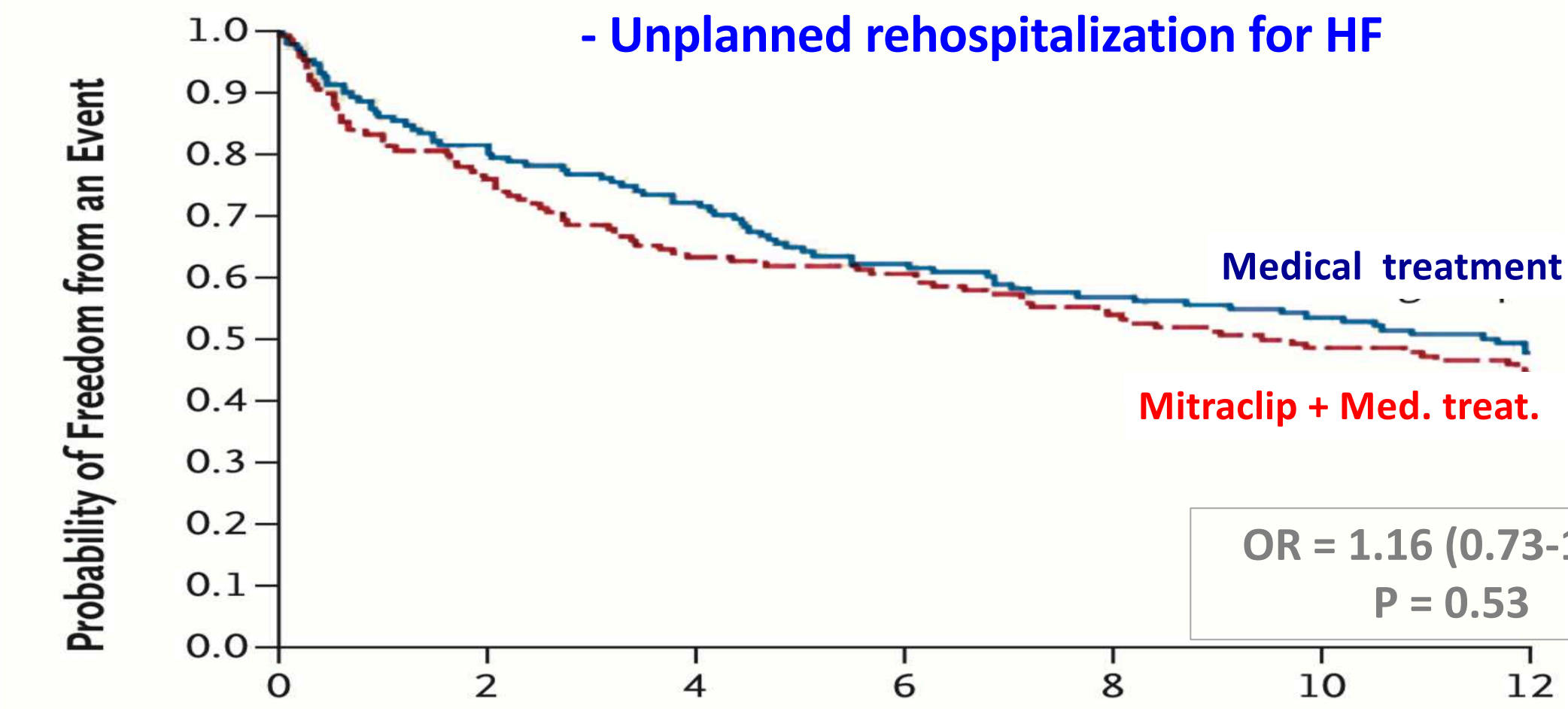
2/3

EF=33%

S=31mm^2

Primary composite endpoint *(99% follow-up)*

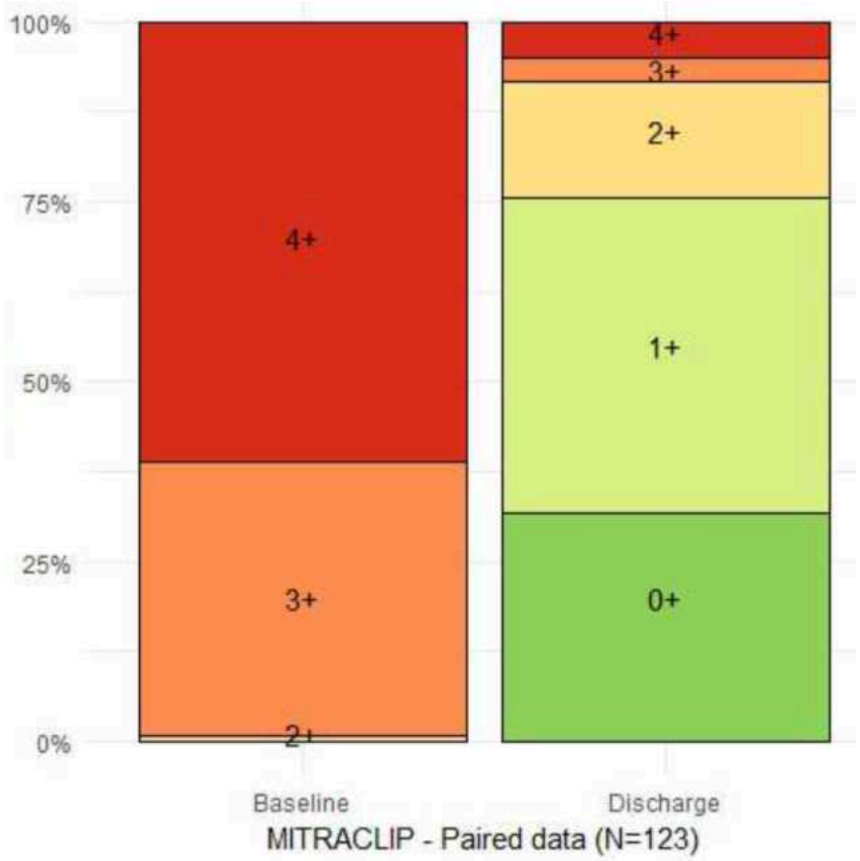
- All-Cause Death
- Unplanned rehospitalization for HF

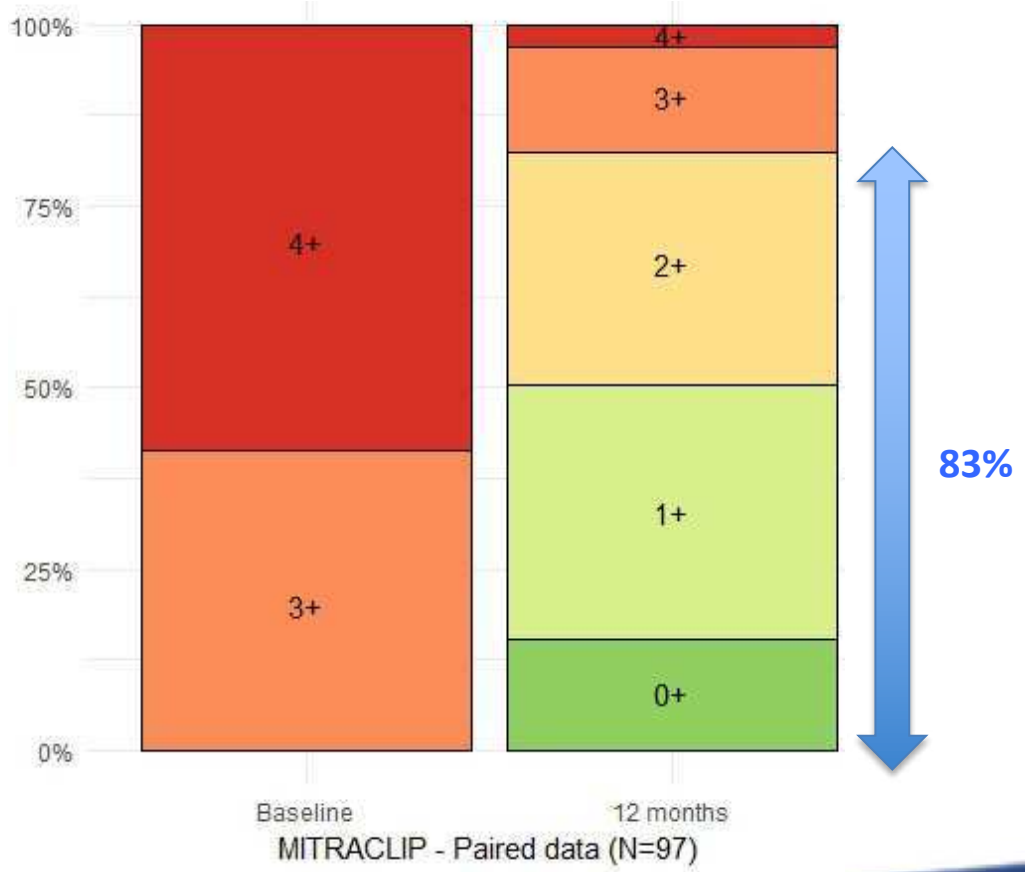


OR = 1.16 (0.73-1.84)
P = 0.53

Prespecified Secondary Endpoints

MR Grade evolution Corelab





News > Medscape Medical News > Conference News > ESC 2018

MITRA-FR: *MitraClip* Comes Up Empty-Handed in Functional Mitral Regurgitation

Patrice Wendling

August 28, 2018

NEWS • INTERVENTIONAL | ESC 2018

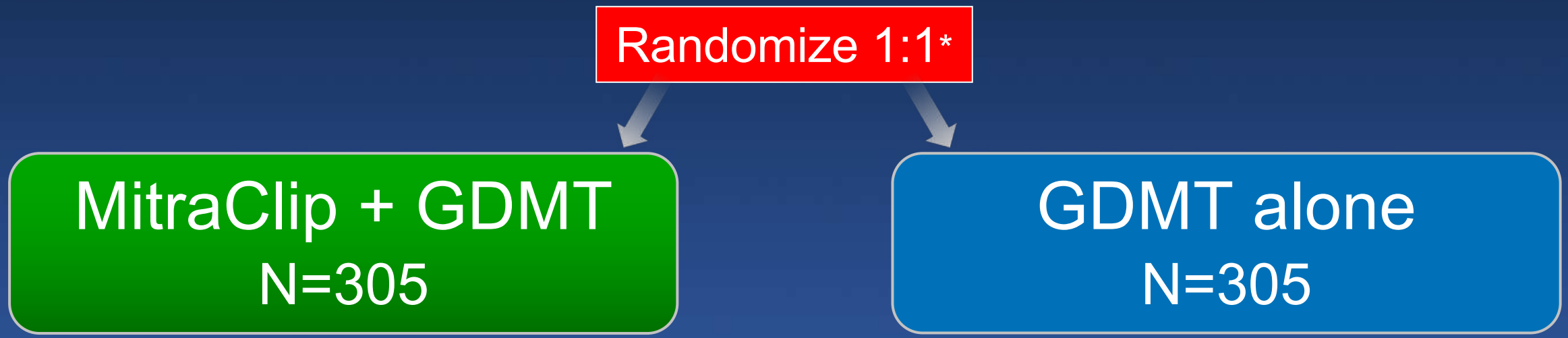
MITRA-FR: No Benefit of MitraClip in Functional MR

Presenting the results today, Jean-François Obadia expressed hope that other trials will help identify patients who might benefit from the device.

The COAPT Trial

Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation

A parallel-controlled, open-label, multicenter trial in ~610 patients with heart failure and moderate-to-severe (3+) or severe (4+) secondary MR who remained symptomatic despite maximally-tolerated GDMT



*Stratified by cardiomyopathy etiology (ischemic vs. non-ischemic) and site

COAPT TRIAL

Key Inclusion Criteria

1. Ischemic or non-ischemic cardiomyopathy with LVEF 20%-50% and LVESD ≤70 mm
2. Moderate-to-severe (3+) or severe (4+) secondary MR confirmed by an independent echo core laboratory prior to enrollment (US ASE criteria)
3. NYHA functional class II-IVa (ambulatory) despite a stable maximally-tolerated GDMT regimen and CRT (if appropriate) per societal guidelines
4. Pt has had at least one HF hospitalization within 12 months and/or a BNP ≥300 pg/ml* or a NT-proBNP ≥1500 pg/ml*
5. Not appropriate for mitral valve surgery by local heart team assessment
6. IC believes secondary MR can be successfully treated by the MitraClip

Adjusted by a 4% reduction in the BNP or NT-proBNP cutoff for every increase of 1 kg/m^2 in BMI >20 kg/m^2

COAPT TRIAL

Key Exclusion Criteria

1. ACC/AHA stage D HF, hemodynamic instability or cardiogenic shock
2. Untreated clinically significant CAD requiring revascularization
3. COPD requiring continuous home oxygen or chronic oral steroid use
4. Severe pulmonary hypertension or moderate or severe right ventricular dysfunction
5. Aortic or tricuspid valve disease requiring surgery or transcatheter intervention
6. Mitral valve orifice area <4.0 cm^2 by site-assessed TTE
7. Life expectancy <12 months due to non-cardiac conditions

COAPT TRIAL

Primary Endpoints

Primary effectiveness endpoint: All HF hospitalizations through 24 months*

Powered for superiority of the Device group compared with the Control group

Primary safety endpoint: Freedom at 12 mos from device-related complications:

- Single leaflet device attachment
- Device embolization
- Endocarditis requiring surgery
- Echo core laboratory-confirmed mitral stenosis requiring surgery
- Left ventricular assist device implant
- Heart transplant
- Any device-related complication requiring non-elective cardiovascular surgery

Powered for superiority of the Device group vs. a pre-specified OPG**

*Analyzed when the last subject completes 12 months of follow-up; **Objective performance goal

Study Flow and Follow-up

1576 pts with HF and MR considered for enrollment between September 25th, 2012 and June 23th, 2017 at 89 centers in the US and Canada

Ineligible
N=911

Reasons for exclusion
Inadequate MR or DMR (n=244)
Not treated with GDMT (n=79)
All inclusion criteria not met (n=85)
Exclusion criteria present (n=34)
Echo criteria not met (n=255)
Incomplete screening
or other (n=419)

Eligible for enrollment
N=665

Roll-in cases
N=51 at 34 sites

Randomized
N=614 at 78 sites

MitraClip + GDMT
N=302

GDMT alone
N=312

COAPT TRIAL

Baseline Characteristics (i)

	MitraClip + GDMT (N=302)	GDMT alone (N=312)
Age (years)	71.7 ± 11.8	72.8 ± 10.5
Male	66.6%	61.5%
Diabetes	35.1%	39.4%
Hypertension	80.5%	80.4%
Hyperchol.	55.0%	52.2%
Prior MI	51.7%	51.3%
Prior PCI	43.0%	49.0%
Prior CABG	40.1%	40.4%
Prior stroke or TIA	18.5%	15.7%
PVD	17.2%	18.3%
COPD	23.5%	23.1%
H/o atrial fibr	57.3%	53.2%

	MitraClip + GDMT (N=302)	GDMT alone (N=312)
BMI (kg/m^2)	27.0 ± 5.8	27.1 ± 5.9
CrCl (ml/min)	50.9 ± 28.5	47.8 ± 25.0
- ≤60 ml/min	71.6%	75.2%
Anemia (WHO)	59.8%	62.7%
BNP (pg/mL)	1015 ± 1086	1017 ± 1219
NT-proBNP (pg/mL)	5174 ± 6567	5944 ± 8438
STS replacement sc	7.8 ± 5.5	8.5 ± 6.2
- ≥8	41.7%	43.6%
Surgical risk (central eligibility committee)		
- High*	68.6%	69.9%
- Not-high	31.4%	30.1%

* STS repl score ≥8% or one or more factors present predicting extremely high surgical risk

COAPT TRIAL

Baseline Characteristics (ii)

HF parameters	MitraClip + GDMT (N=302)	GDMT alone (N=312)
Etiology of HF		
- Ischemic	60.9%	60.6%
- Non-ischemic	39.1%	39.4%
NYHA class		
- I	0.3%	0%
- II	42.7%	35.4%
- III	51.0%	54.0%
- IV	6.0%	10.6%
HF hosp w/i 1 year	58.3%	56.1%
Prior CRT	38.1%	34.9%
Prior defibrillator	30.1%	32.4%

Echo core lab	MitraClip + GDMT (N=302)	GDMT alone (N=312)
MR severity		
- Mod-to-sev (3+)	49.0%	55.3%
- Severe (4+)	51.0%	44.7%
EROA, cm^2	0.41 ± 0.15	0.40 ± 0.15
LVESD, cm	5.3 ± 0.9	5.3 ± 0.9
LVEDD, cm	6.2 ± 0.7	6.2 ± 0.8
LVESV, mL	135.5 ± 56.1	134.3 ± 60.3
LVEDV, mL	194.4 ± 69.2	191.0 ± 72.9
LVEF, %	31.3 ± 9.1	31.3 ± 9.6
- ≤40%	82.2%	82.0%
RVSP, mmHg	44.0 ± 13.4	44.6 ± 14.0

COAPT TRIAL

Medication Use at Baseline

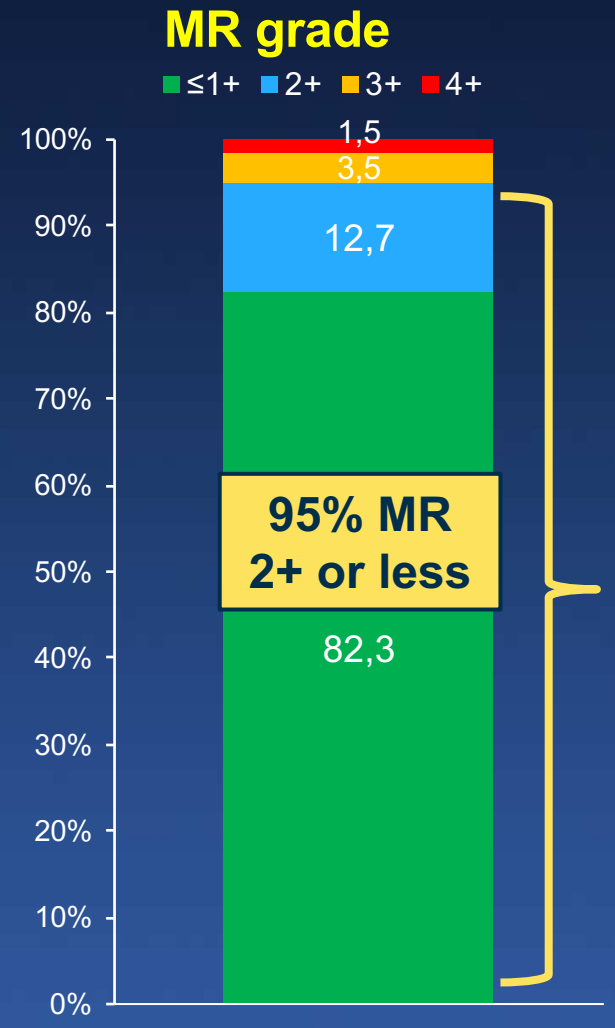
Maximally-tolerated doses	MitraClip + GDMT (n=302)	GDMT alone (n=312)
Beta-blocker	91.1%	89.7%
ACEI, ARB or ARNI	71.5%	62.8%
Mineralocorticoid receptor antagonist	50.7%	49.7%
Nitrates	6.3%	8.0%
Hydralazine	16.6%	17.6%
Diuretic	89.4%	88.8%
Chronic oral anticoagulant	46.4%	40.1%
Aspirin	57.6%	64.7%
P2Y12 receptor inhibitor	25.2%	22.8%
Statin	62.6%	60.6%

COAPT TRIAL

MitraClip Procedure (n=302)

MitraClip procedure attempted	293/302 (97.0%)
Clip implanted (MitraClip procedure attempted)	287/293 (98.0%)
Clip implanted (all patients)	287/302 (95.0%)
Mean # of clips implanted	1.7 ± 0.7 (n=293)
- 0 clips implanted	6 (2.0%)
- 1 clip implanted	106 (36.2%)
- 2 clips implanted	157 (53.6%)
- 3 clips implanted	23 (7.9%)
- 4 clips implanted	1 (0.3%)
Procedure duration (mins)	162.9 ± 118.1
- Device procedure time (mins)	118.9 ± 63.5
- Device time (mins)	82.7 ± 80.8
- Fluoroscopy time (mins)	33.9 ± 23.2

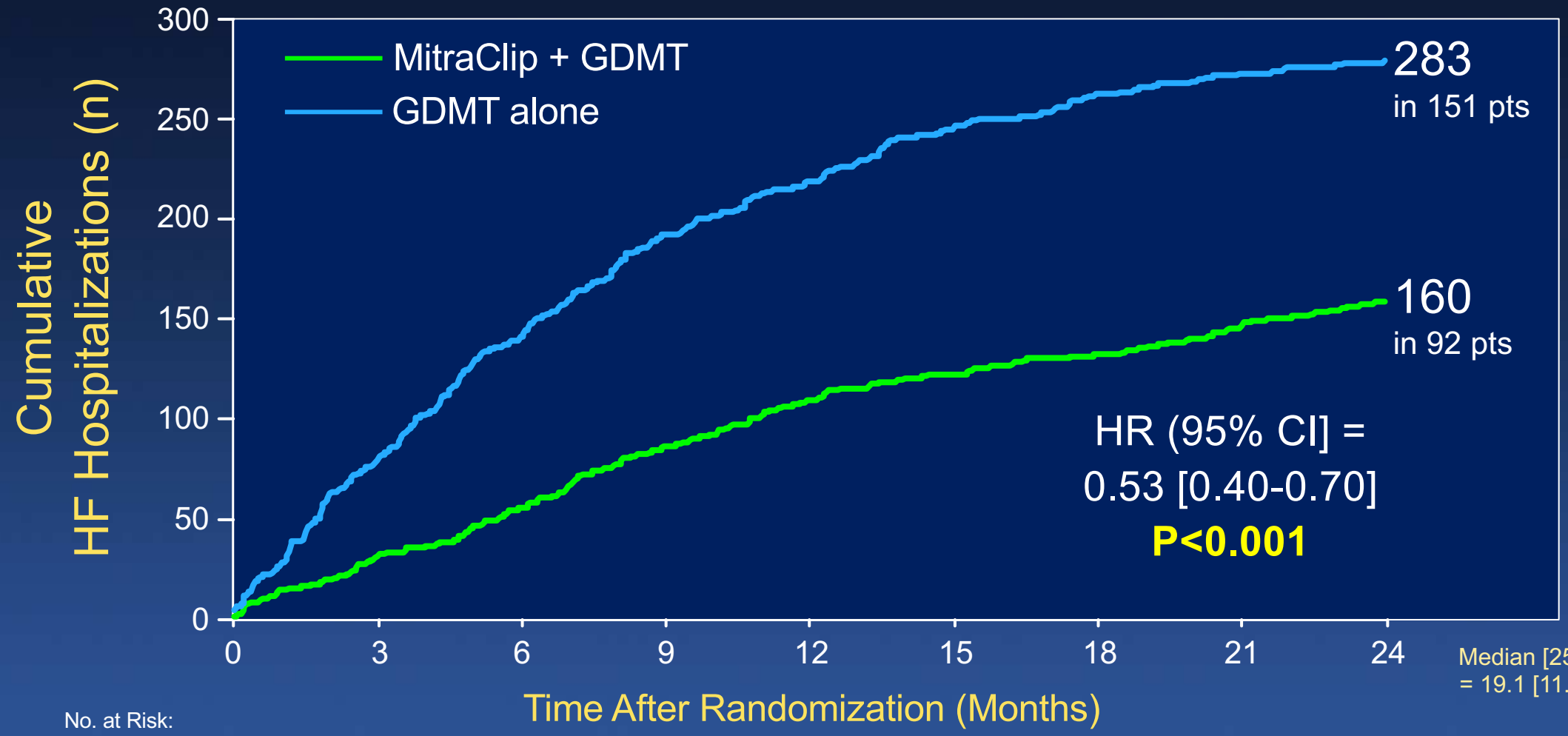
TTE at discharge (n=260)



COAPT TRIAL

Primary Effectiveness Endpoint

All Hospitalizations for HF within 24 months



Median [25%, 75%] FU = 19.1 [11.9, 24.0] mos

No. at Risk:

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

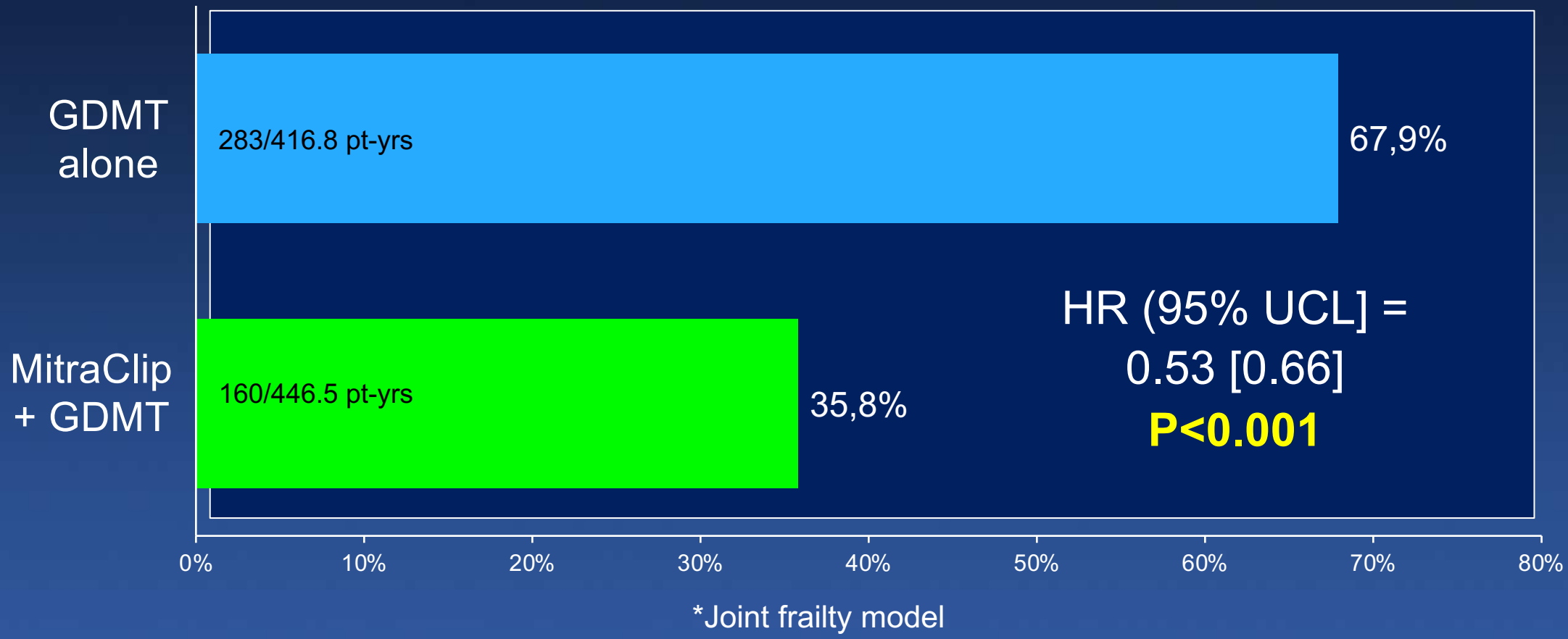
COAPT TRIAL

Primary Effectiveness Endpoint

Hospitalizations for HF within 24 months

Annualized rates of HF hospitalization*

NNT (24 mo) = 3.1 [95% CI 1.9, 8.2]



*Joint frailty model

Powered Secondary Endpoints

- Tested in hierarchical order[1] -

	P-value
1. MR grade ≤2+ at 12 months	
2. All-cause mortality at 12 months[2]	
3. Death and all HF hospitalization through 24 months (Finkelstein-Schoenfeld)	
4. Change in QOL (KCCQ) from baseline to 12 months	
5. Change in 6MWD from baseline to 12 months	
6. All-cause hospitalizations through 24 months	
7. NYHA class I or II at 12 months	
8. Change in LVEDV from baseline to 12 months	
9. All-cause mortality at 24 months	
10. Death, stroke, MI, or non-elective CV surgery for device-related compls at 30 days[3]	

vs. the control group; [3]Powered for noninferiority against an objective performance goal

COAPT TRIAL

Powered Secondary Endpoints

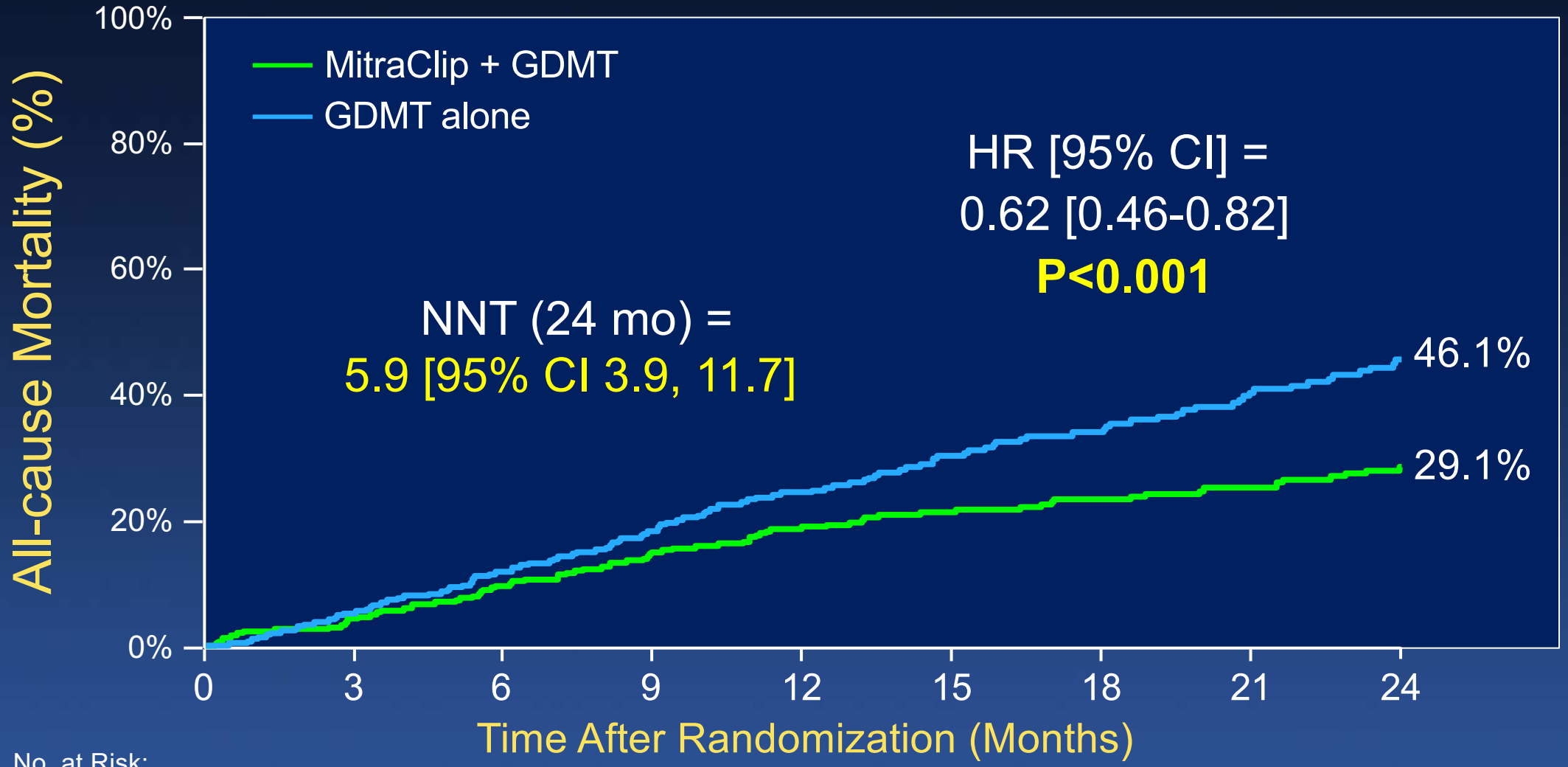
- Tested in hierarchical order[1] -

	P-value
1. MR grade ≤2+ at 12 months	<0.001
2. All-cause mortality at 12 months[2]	<0.001
3. Death and all HF hospitalization through 24 months (Finkelstein-Schoenfeld)	<0.001
4. Change in QOL (KCCQ) from baseline to 12 months	<0.001
5. Change in 6MWD from baseline to 12 months	<0.001
6. All-cause hospitalizations through 24 months	0.03
7. NYHA class I or II at 12 months	<0.001
8. Change in LVEDV from baseline to 12 months	0.003
9. All-cause mortality at 24 months	<0.001
10. Death, stroke, MI, or non-elective CV surgery for device-related compls at 30 days[3]	<0.001

[1]All powered for superiority unless otherwise noted; [2]Powered for noninferiority of the device vs. the control group; [3]Powered for noninferiority against an objective performance goal

COAPT TRIAL

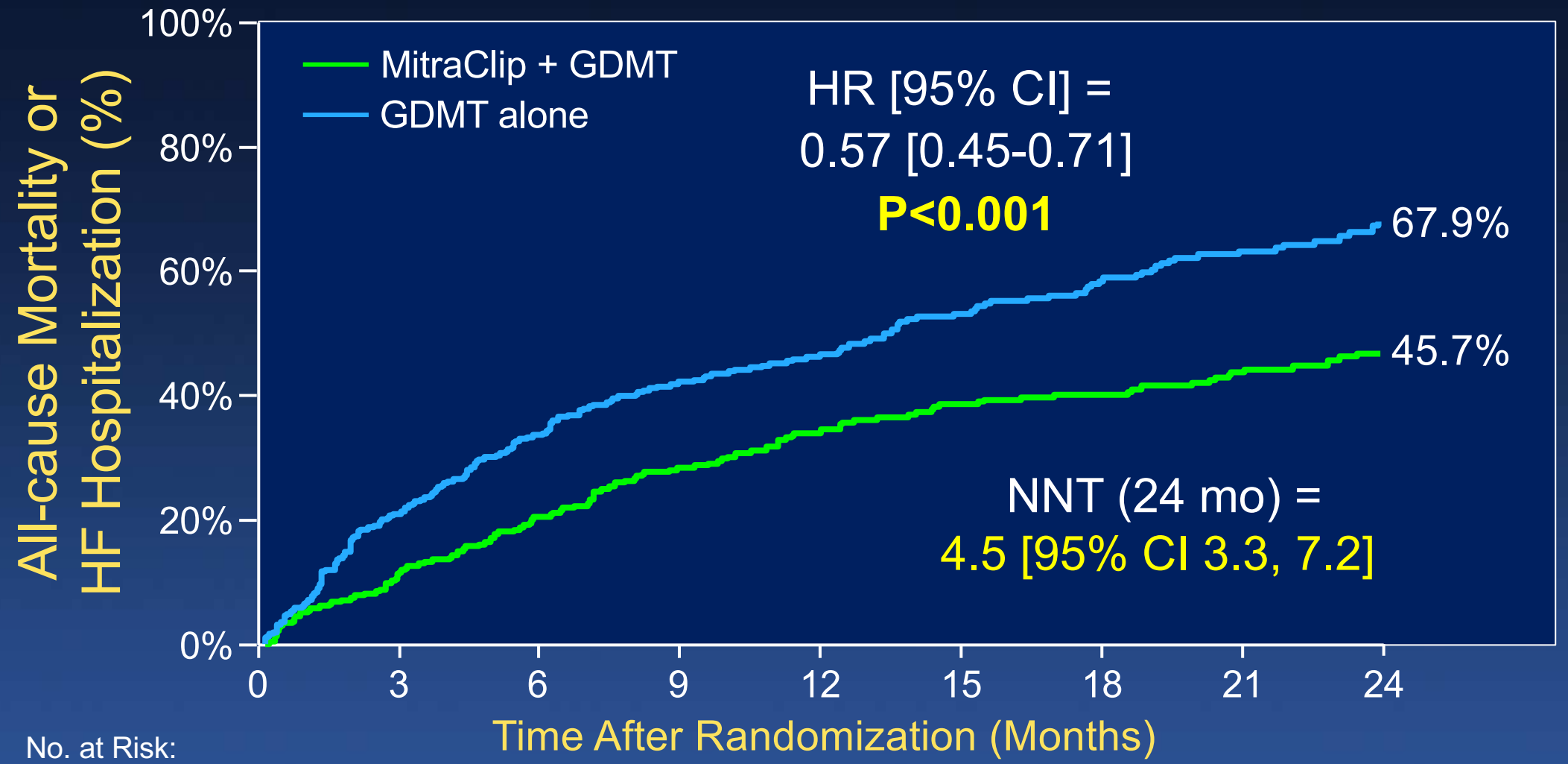
All-cause Mortality



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

COAPT TRIAL

Death or HF Hospitalization



No. at Risk:

MitraClip + GDMT	302	264	238	215	194	154	145	126	97
GDMT alone	312	244	205	174	153	117	90	75	55

COAPT TRIAL

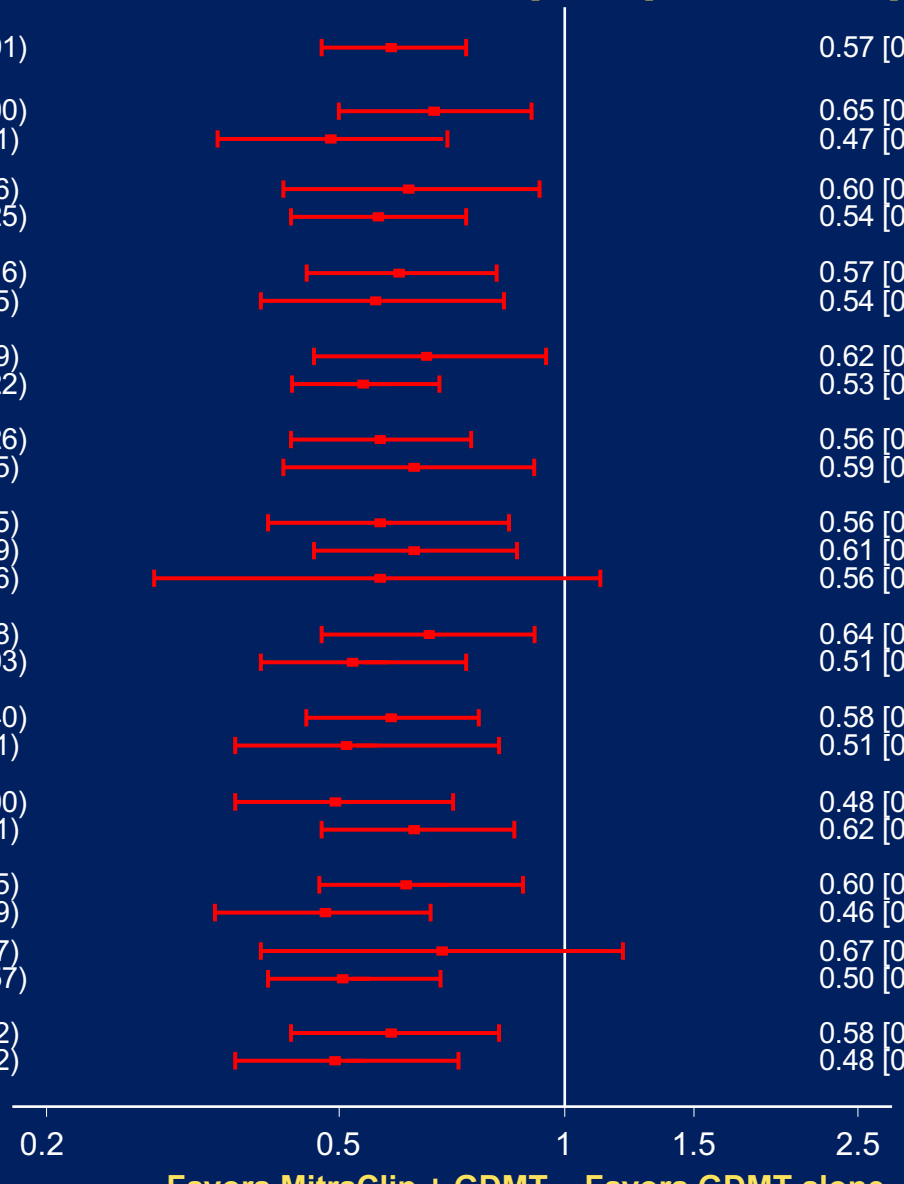
Major Changes in HF Meds w/i 12 Months

	MitraClip + GDMT (n=302)	GDMT alone (n=312)	P value
ACEI, ARB or ARNI			
- ⇓ dose by >50% or discontinue	6.6%	4.8%	0.33
- ⇑ dose by >100% or new drug started	7.6%	7.4%	0.91
Beta-blocker			
- ⇓ dose by >50% or discontinue	5.3%	5.1%	0.92
- ⇑ dose by >100% or new drug started	8.6%	3.8%	0.01
Mineralocorticoid receptor antagonist			
- ⇓ dose by >50% or discontinue	0.7%	0.6%	1.00
- ⇑ dose by >100% or new drug started	5.3%	2.6%	0.08
Nitrates			
- ⇓ dose by >50% or discontinue	0.0%	0.0%	1.00
- ⇑ dose by >100% or new drug started	1.0%	1.9%	0.51
Hydralazine			
- ⇓ dose by >50% or discontinue	1.0%	0.0%	0.12
- ⇑ dose by >100% or new drug started	4.3%	3.8%	0.77

COAPT TRIAL

24-Month Death or HF Hospitalization

Subgroup	MitraClip + GDMT	GDMT alone	HR [95% CI]	P [Int]
All patients	45.7% (129)	67.9% (191)	0.57 [0.45, 0.71]	
Age (median)				
≥74 years (n=317)	52.1% (78)	70.2% (100)	0.65 [0.48, 0.88]	0.13
<74 years (n=297)	37.8% (51)	65.3% (91)	0.47 [0.33, 0.66]	
Sex				
Female (n=221)	43.2% (39)	59.4% (66)	0.60 [0.40, 0.89]	0.76
Male (n=393)	47.1% (90)	73.0% (125)	0.54 [0.41, 0.71]	
Etiology of cardiomyopathy				
Ischemic (n=373)	48.1% (84)	70.0% (116)	0.57 [0.43, 0.76]	0.79
Non-ischemic (n=241)	41.1% (45)	65.2% (75)	0.54 [0.37, 0.78]	
Prior CRT				
Yes (n=224)	50.2% (55)	68.4% (69)	0.62 [0.44, 0.89]	0.54
No (n=390)	42.9% (74)	67.4% (122)	0.53 [0.39, 0.71]	
HF hospitalization within the prior year				
Yes (n=407)	44.7% (86)	67.9% (126)	0.56 [0.42, 0.73]	0.79
No (n=207)	47.6% (43)	67.8% (65)	0.59 [0.40, 0.86]	
Baseline NYHA class				
I or II (n=240)	41.1% (50)	66.9% (65)	0.56 [0.39, 0.81]	0.92
III (n=322)	46.6% (67)	65.3% (99)	0.61 [0.44, 0.83]	
IV (n=51)	68.3% (12)	84.4% (26)	0.56 [0.28, 1.12]	
STS replacement score				
≥8% (n=262)	54.1% (65)	71.4% (88)	0.64 [0.46, 0.88]	0.41
<8% (n=352)	39.2% (64)	65.0% (103)	0.51 [0.37, 0.70]	
Surgical risk status*				
High (n=423)	49.7% (95)	71.5% (140)	0.58 [0.45, 0.75]	0.69
Not high (n=188)	35.8% (32)	58.7% (51)	0.51 [0.33, 0.80]	
Baseline MR grade				
3+ (n=320)	37.5% (51)	65.3% (100)	0.48 [0.34, 0.67]	0.29
4+ (n=293)	53.4% (78)	71.4% (91)	0.62 [0.45, 0.83]	
Baseline LVEF				
≥30% (median; n=301)	44.1% (62)	61.2% (85)	0.60 [0.43, 0.84]	0.32
<30% (median; n=274)	46.4% (56)	77.8% (99)	0.46 [0.33, 0.64]	
>40% (n=103)	49.7% (22)	56.2% (27)	0.67 [0.38, 1.17]	0.31
≤40% (n=472)	44.2% (96)	71.9% (157)	0.50 [0.39, 0.65]	
Baseline LVEDV (median)				
≥181 mL (n=288)	48.9% (43)	68.0% (92)	0.58 [0.42, 0.80]	0.42
<181 mL (n=287)	41.5% (54)	69.5% (92)	0.48 [0.34, 0.67]	



KM time-to-first event rates

*Central eligibility committee assessment

COAPT TRIAL

MR Severity (Core Lab)

MR grade	≤1+	2+	3+	4+	P_{trend}	≤2+	P-value
Baseline							
MitraClip (n=302)	-	-	49.0%	51.0%	-	-	-
GDMT (n=311)	-	-	55.3%	44.7%		-	
30 days							
MitraClip (n=273)	72.9%	19.8%	5.9%	1.5%	<0.001	92.7%	<0.001
GDMT (n=257)	8.2%	26.1%	37.4%	28.4%		34.2%	
6 months							
MitraClip (n=240)	66.7%	27.1%	4.6%	1.7%	<0.001	93.8%	<0.001
GDMT (n=218)	9.2%	28.9%	42.2%	19.7%		38.1%	
12 months							
MitraClip (n=210)	69.1%	25.7%	4.3%	1.0%	<0.001	94.8%	<0.001
GDMT (n=175)	11.4%	35.4%	34.3%	18.9%		46.9%	
24 months							
MitraClip (n=114)	77.2%	21.9%	0%	0.9%	<0.001	99.1%	<0.001
GDMT (n=76)	15.8%	27.6%	40.8%	15.8%		43.4%	

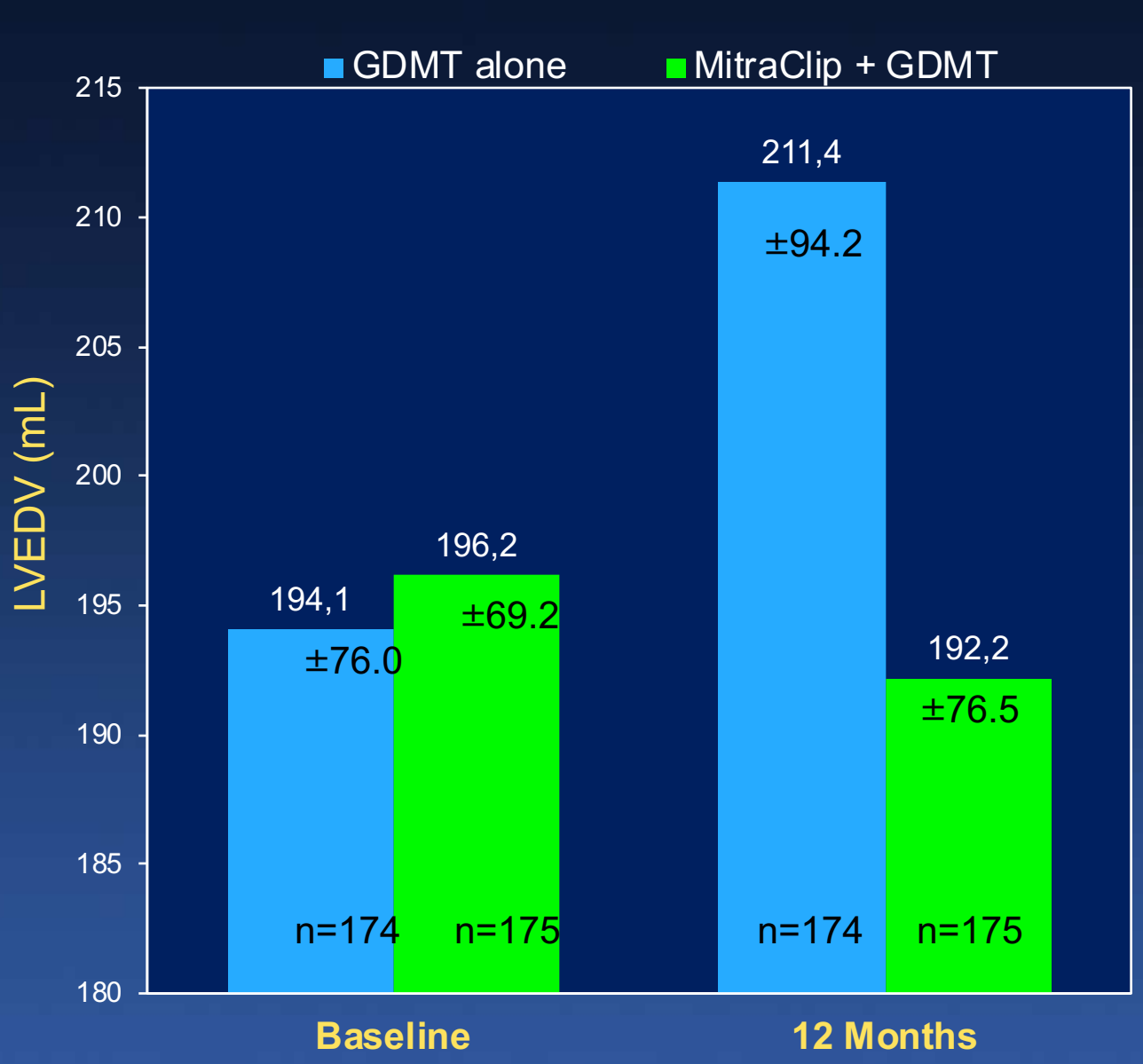
COAPT TRIAL

MR Severity (Core Lab)

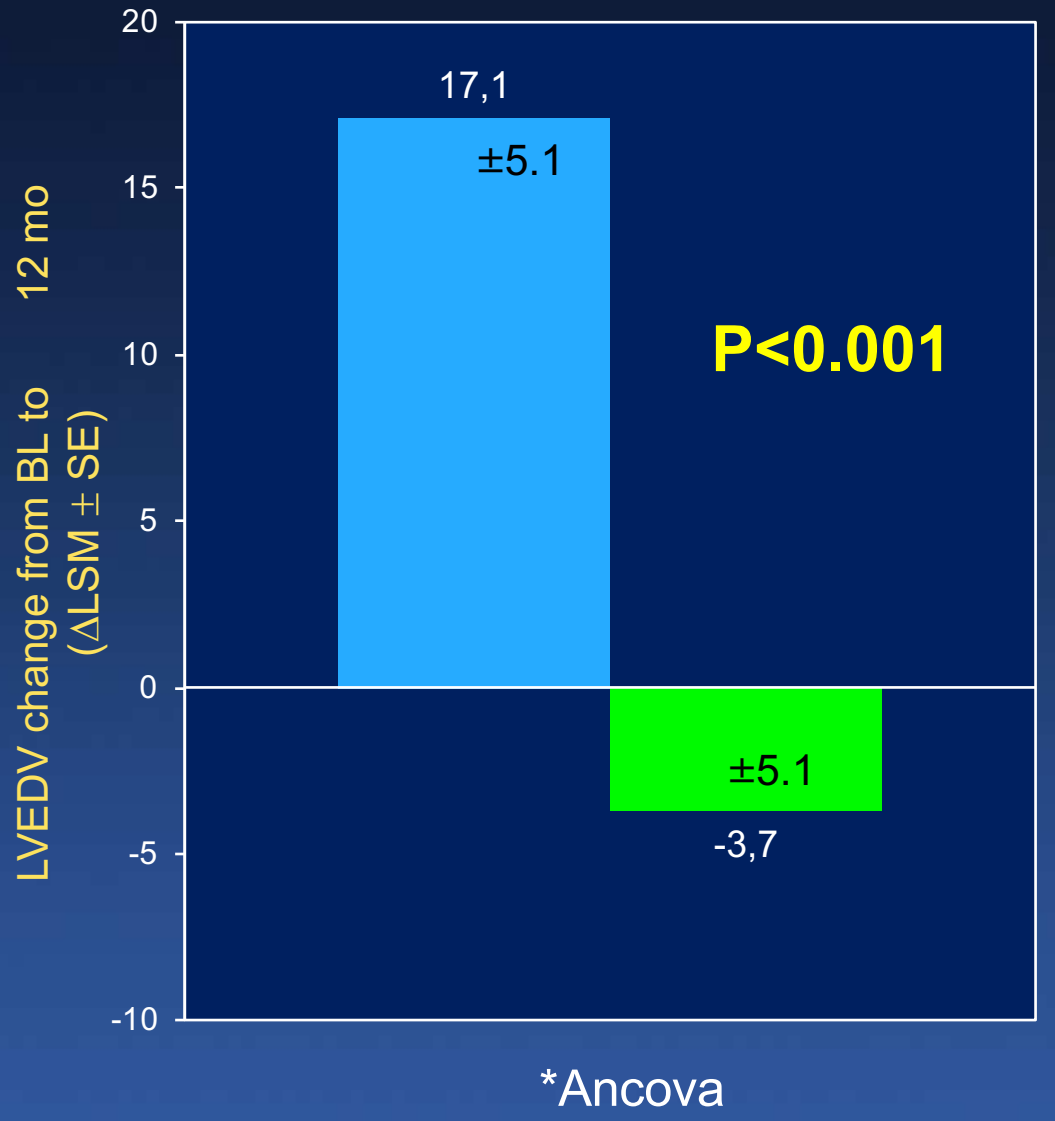
MR grade	≤1+	2+	3+	4+	P_{trend}	≤2+	P-value
Baseline							
MitraClip (n=302)	-	-	49.0%	51.0%	-	-	-
GDMT (n=311)	-	-	55.3%	44.7%		-	
30 days							
MitraClip (n=273)	72.9%	19.8%	5.9%	1.5%	<0.001	92.7%	<0.001
GDMT (n=257)	8.2%	26.1%	37.4%	28.4%		34.2%	
6 months							
MitraClip (n=240)	66.7%	27.1%	4.6%	1.7%	<0.001	93.8%	<0.001
GDMT (n=218)	9.2%	28.9%	42.2%	19.7%		38.1%	
12 months							
MitraClip (n=210)	69.1%	25.7%	4.3%	1.0%	<0.001	94.8%	<0.001
GDMT (n=175)	11.4%	35.4%	34.3%	18.9%		46.9%	
24 months							
MitraClip (n=114)	77.2%	21.9%	0%	0.9%	<0.001	99.1%	<0.001
GDMT (n=76)	15.8%	27.6%	40.8%	15.8%		43.4%	

COAPT TRIAL

Change in LVEDV from Baseline to 12 Months

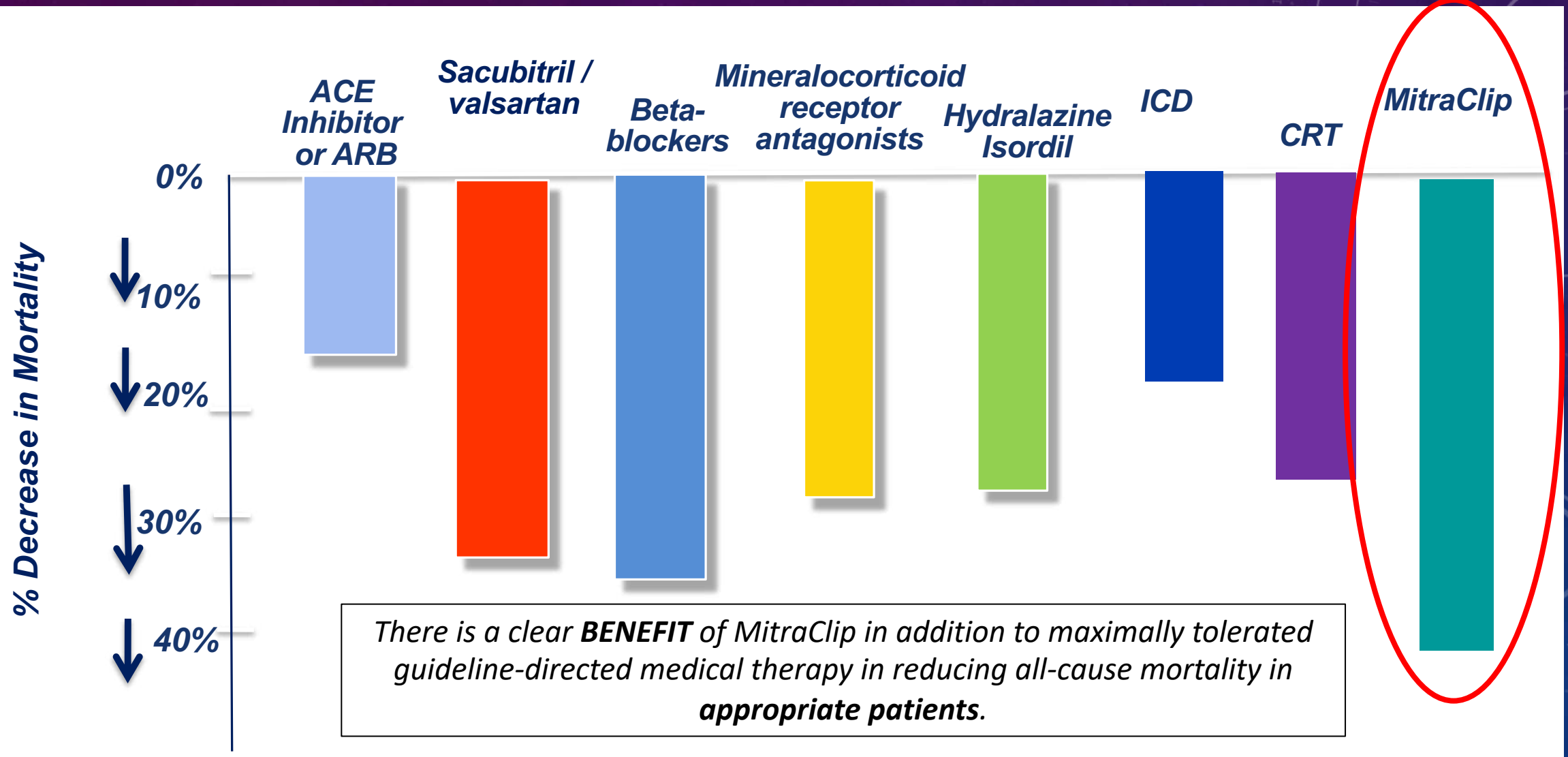


Adjusted change*



*Ancova

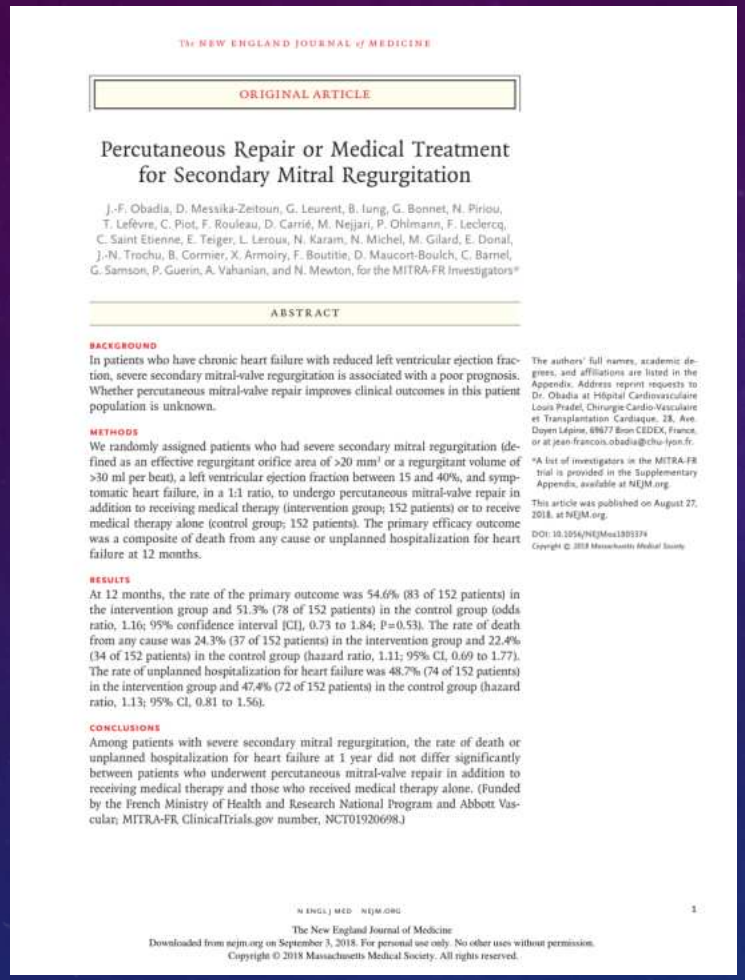
Mortality benefits of Therapies for HFrEF



*There is a clear **BENEFIT** of MitraClip in addition to maximally tolerated guideline-directed medical therapy in reducing all-cause mortality in **appropriate patients**.*

Courtesy of Joann Lindenfeld

Secondary Mitral Regurgitation



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. 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*

ABSTRACT

BACKGROUND

In patients who have chronic heart failure with reduced left ventricular ejection fraction, severe secondary mitral-valve regurgitation is associated with a poor prognosis. Whether percutaneous mitral-valve repair improves clinical outcomes in this patient population is unknown.

METHODS

We randomly assigned patients who had severe secondary mitral regurgitation (defined as an effective regurgitant orifice area of >20 mm² or a regurgitant volume of >30 ml per beat), a left ventricular ejection fraction between 15 and 40%, and symptomatic heart failure, in a 1:1 ratio, to undergo percutaneous mitral-valve repair in addition to receiving medical therapy (intervention group; 152 patients) or to receive medical therapy alone (control group; 152 patients). The primary efficacy outcome was a composite of death from any cause or unplanned hospitalization for heart failure at 12 months.

RESULTS

At 12 months, the rate of the primary outcome was 54.6% (83 of 152 patients) in the intervention group and 51.3% (78 of 152 patients) in the control group (odds ratio, 1.16; 95% confidence interval [CI], 0.73 to 1.84; P=0.53). The rate of death from any cause was 24.3% (37 of 152 patients) in the intervention group and 22.4% (34 of 152 patients) in the control group (hazard ratio, 1.11; 95% CI, 0.69 to 1.77). The rate of unplanned hospitalization for heart failure was 48.7% (74 of 152 patients) in the intervention group and 47.4% (72 of 152 patients) in the control group (hazard ratio, 1.13; 95% CI, 0.81 to 1.56).

CONCLUSIONS

Among patients with severe secondary mitral regurgitation, the rate of death or unplanned hospitalization for heart failure at 1 year did not differ significantly between patients who underwent percutaneous mitral-valve repair in addition to receiving medical therapy and those who received medical therapy alone. (Funded by the French Ministry of Health and Research National Program and Abbott Vascular; MITRA-FR ClinicalTrials.gov number, NCT01920698.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Obadia at Hôpital Cardiovasculaire Louis Pradel, Chirurgie Cardio-Vasculaire et Transplantation Cardiaque, 28, Ave. Doyen Lépine, 69677 Bron CEDEX, France, or at jean-francois.obadia@chu-lyon.fr.

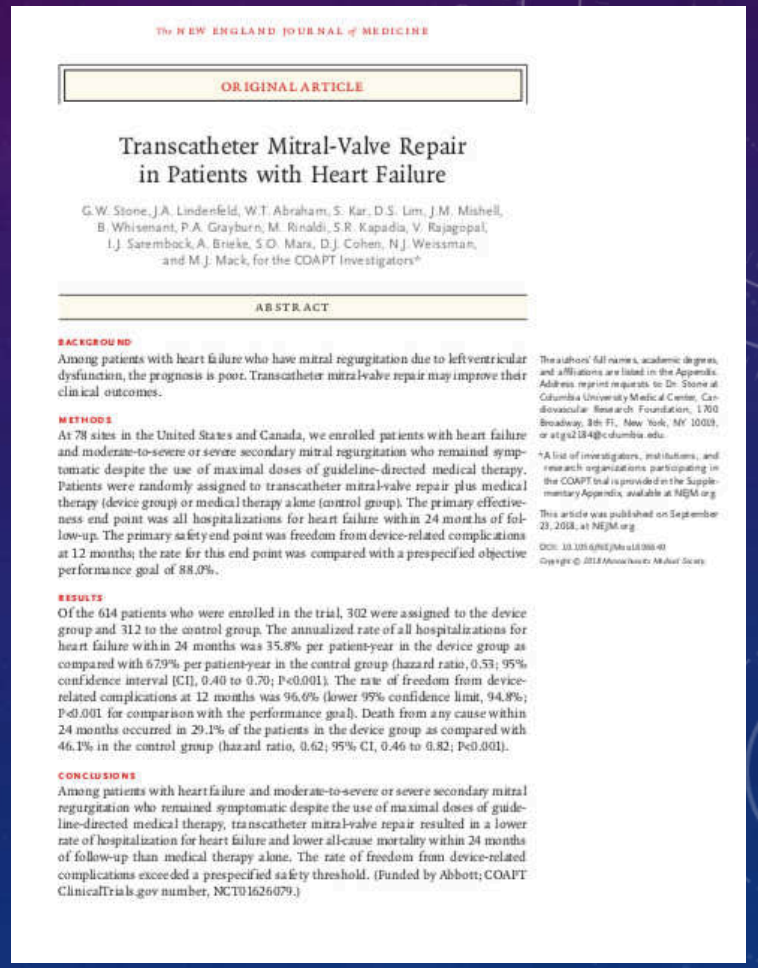
*A list of investigators in the MITRA-FR trial is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on August 27, 2018, at NEJM.org.

DOI: 10.1056/NEJMoa1805374

MITRA-FR
August 2018

VS.



The NEW ENGLAND JOURNAL of MEDICINE

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*

ABSTRACT

BACKGROUND

Among patients with heart failure who have mitral regurgitation due to left ventricular dysfunction, the prognosis is poor. Transcatheter mitral-valve repair may improve their clinical outcomes.

METHODS

At 78 sites in the United States and Canada, we enrolled patients with heart failure and moderate-to-severe or severe secondary mitral regurgitation who remained symptomatic despite the use of maximal doses of guideline-directed medical therapy. Patients were randomly assigned to transcatheter mitral-valve repair plus medical therapy (device group) or medical therapy alone (control group). The primary effectiveness end point was all hospitalizations for heart failure within 24 months of follow-up. The primary safety end point was freedom from device-related complications at 12 months; the rate for this end point was compared with a prespecified objective performance goal of 88.0%.

RESULTS

Of the 614 patients who were enrolled in the trial, 302 were assigned to the device group and 312 to the control group. The annualized rate of all hospitalizations for heart failure within 24 months was 35.8% per patient-year in the device group as compared with 67.9% per patient-year in the control group (hazard ratio, 0.53; 95% confidence interval [CI], 0.40 to 0.70; P<0.001). The rate of freedom from device-related complications at 12 months was 96.6% (lower 95% confidence limit, 94.8%; P<0.001 for comparison with the performance goal). Death from any cause within 24 months occurred in 29.1% of the patients in the device group as compared with 46.1% in the control group (hazard ratio, 0.62; 95% CI, 0.46 to 0.82; P<0.001).

CONCLUSIONS

Among patients with heart failure and moderate-to-severe or severe secondary mitral regurgitation who remained symptomatic despite the use of maximal doses of guideline-directed medical therapy, transcatheter mitral-valve repair resulted in a lower rate of hospitalization for heart failure and lower all-cause mortality within 24 months of follow-up than medical therapy alone. The rate of freedom from device-related complications exceeded a prespecified safety threshold. (Funded by Abbott; COAPT ClinicalTrials.gov number, NCT01626079.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Stone at Columbia University Medical Center, Cardiovascular Research Foundation, 1700 Broadway, 8th Fl., New York, NY 10019, or at gs2184@cumbia.edu.

*A list of investigators, institutions, and research organizations participating in the COAPT trial is provided in the Supplementary Appendix, available at NEJM.org.

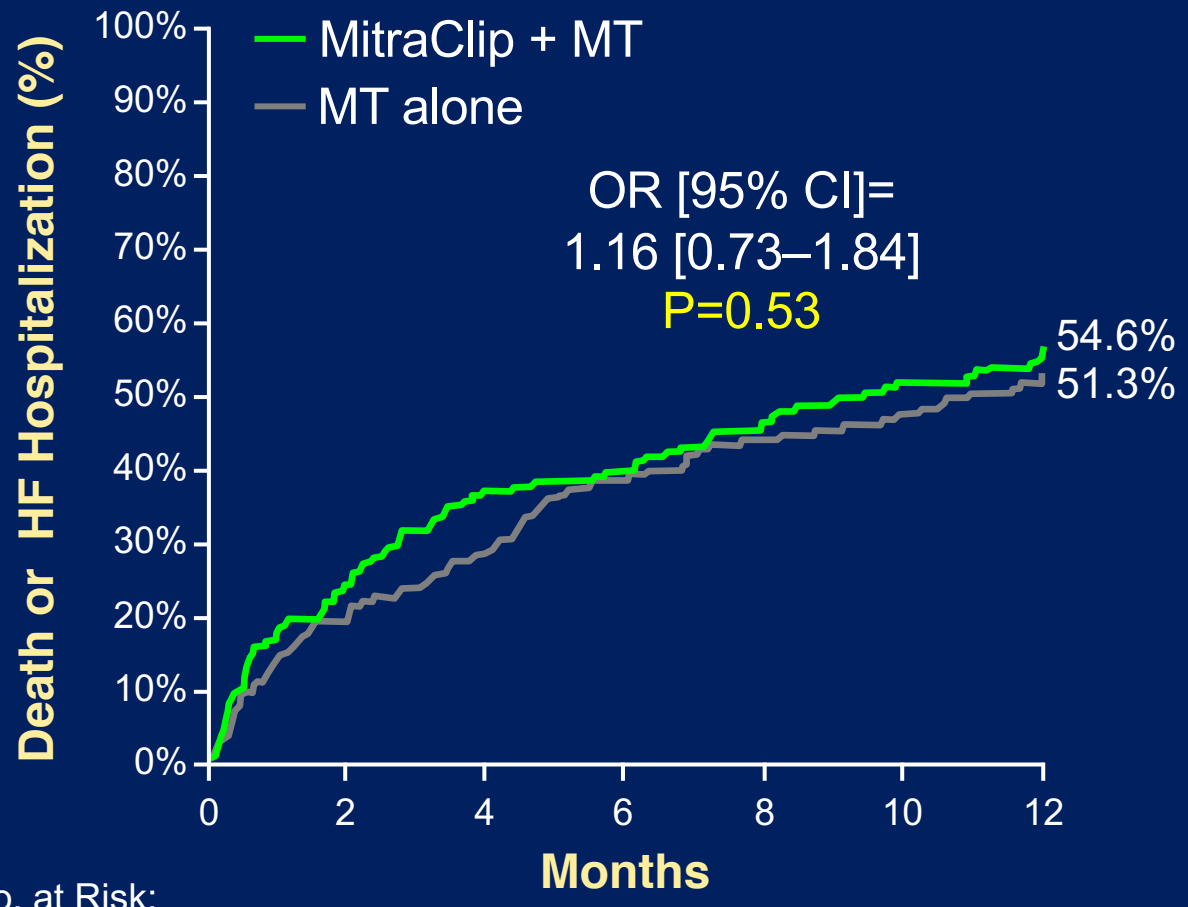
This article was published on September 23, 2018, at NEJM.org.

DOI: 10.1056/NEJMoa1808848

COAPT
September 2018

COAPT vs. MITRA-FR: 12-Month Death or HF Hosp

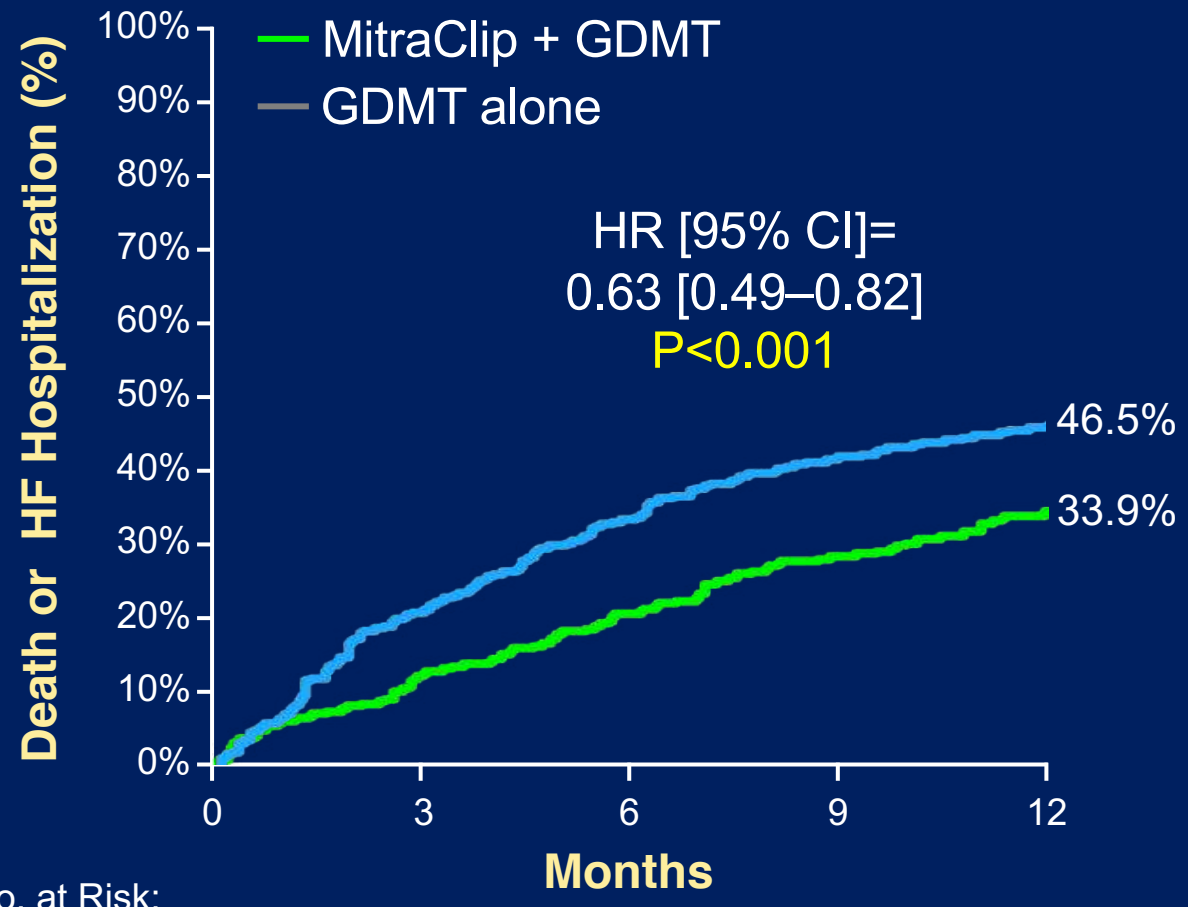
MITRA-FR



No. at Risk:

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

COAPT



No. at Risk:

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

Obadia JF et al. NEJM. 2018 Aug 27. doi: 10.1056/NEJMoa1805374

Stone GW et al. NEJM. 20

INSTITUT DE CARDIOLOGIE DE MONTRÉAL

Affiliée à Université de Montréal

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

Obadia JF et al. NEJM. 2018 Aug 27. doi: 10.1056/NEJMoa1805374; Stone GW et al. NEJM. 2018 Sept

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%)
Procedural complications	25/293 (8.5%)	21/144 (14.6%)
- Device implant failure	6 (2.0%)	6 (4.2%)
- Transfusion or vasc compl requiring surgery	16 (5.5%)	5 (3.5%)
- ASD	2 (0.7%)	4 (2.8%)
- Cardiogenic shock	1 (0.3%)	4 (2.8%)
- 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%

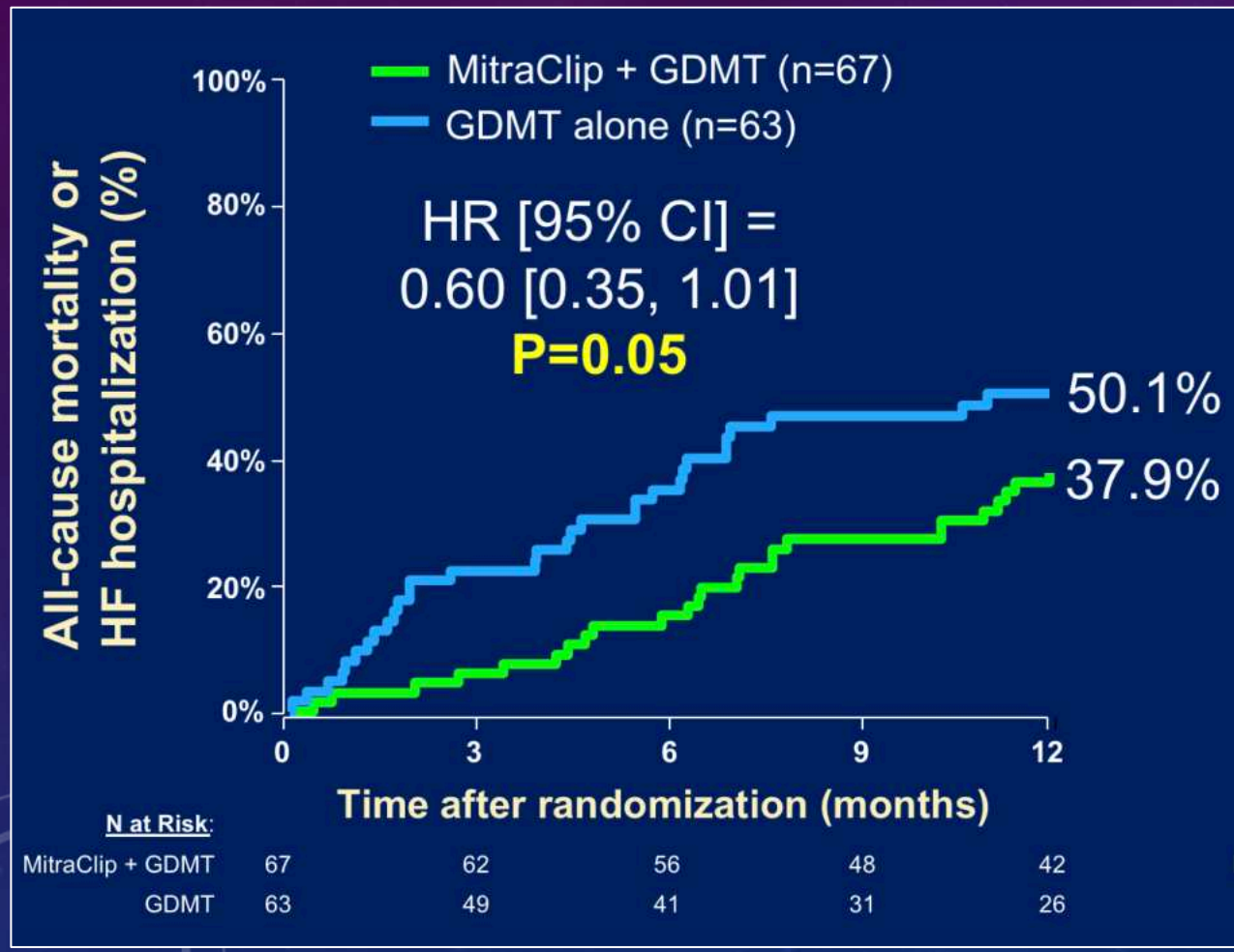
Stone GW et al. NEJM. 2018 Sept 23; Obadia JF et al. NEJM. 2018 Aug 27. doi: 10.1056/NEJMoa1805374

Why are the COAPT Results so Different from MITRA-FR?
Possible Reasons

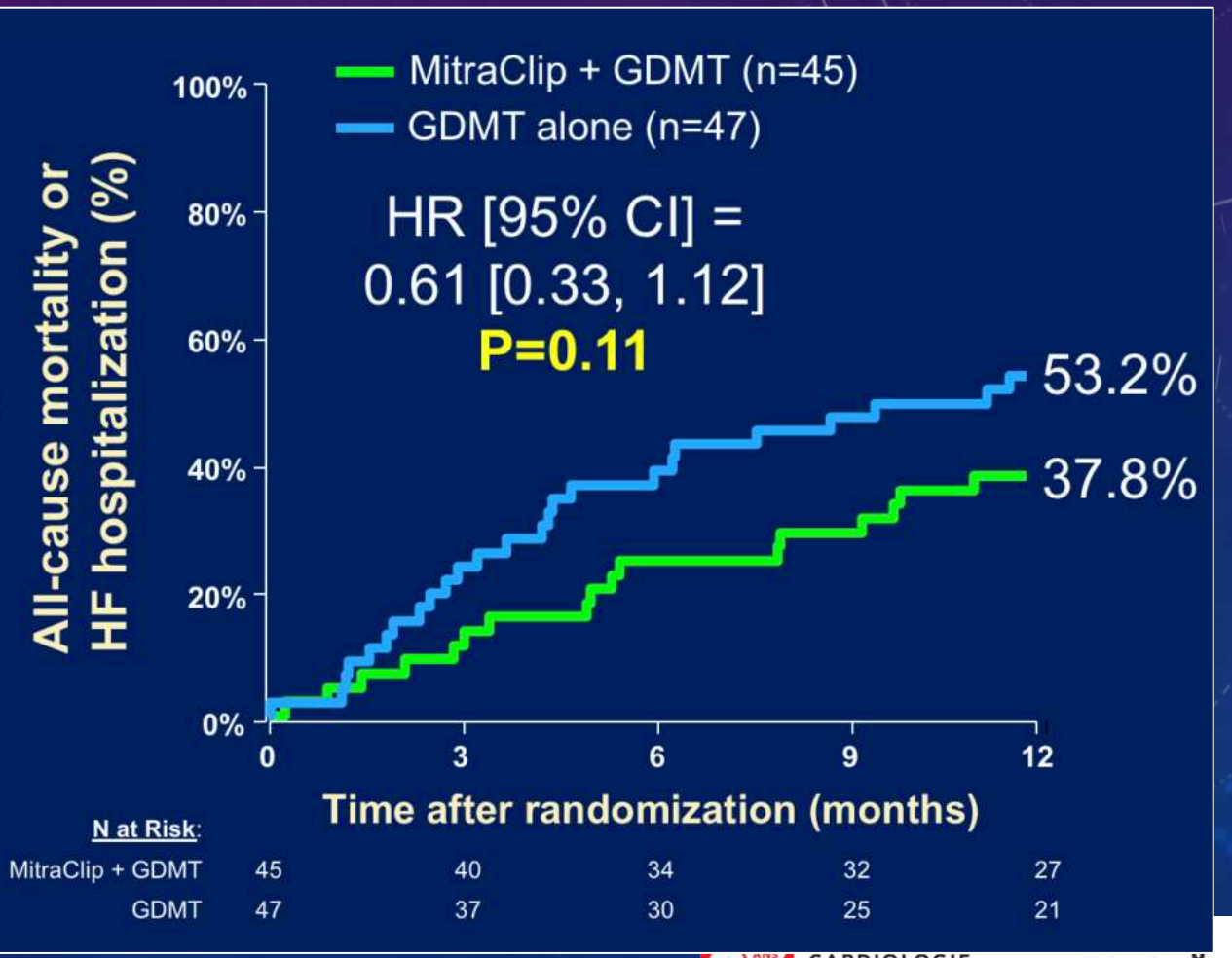
	MITRA-FR (n=304)	COAPT (n=614)
Severe MR entry criteria	Severe FMR by EU guidelines: EROA ERO >20 mm^2 OR RV >30 mL/beat	Severe FMR by US guidelines: EROA >30 mm^2 OR RV >45 mL/beat
EROA (mean ± SD)	31 ± 10 mm^2	41 ± 15 mm^2
LVEDV (mean ± SD)	135 ± 35 mL/m^2	101 ± 34 mL/m^2
GDMT at baseline and FU	Receiving HF meds at baseline – allowed variable adjustment in each group during follow-up per "real-world" practice	CEC confirmed pts were failing maximally-tolerated GDMT at baseline – few major changes during follow-up
Acute results: No clip / ≥3+ MR	9% / 9%	5% / 5%
Procedural complications*	14.6%	8.5%
12-mo MitraClip ≥3+ MR	17%	5%

IMPACT OF EROA AND LVEDV: EROA >40 MM^2
ALL-CAUSE MORTALITY OR HF HOSPITALIZATION THROUGH 12 MONTHS

LVEDVI >96 ml/m^2 (N=130; 23.7%)

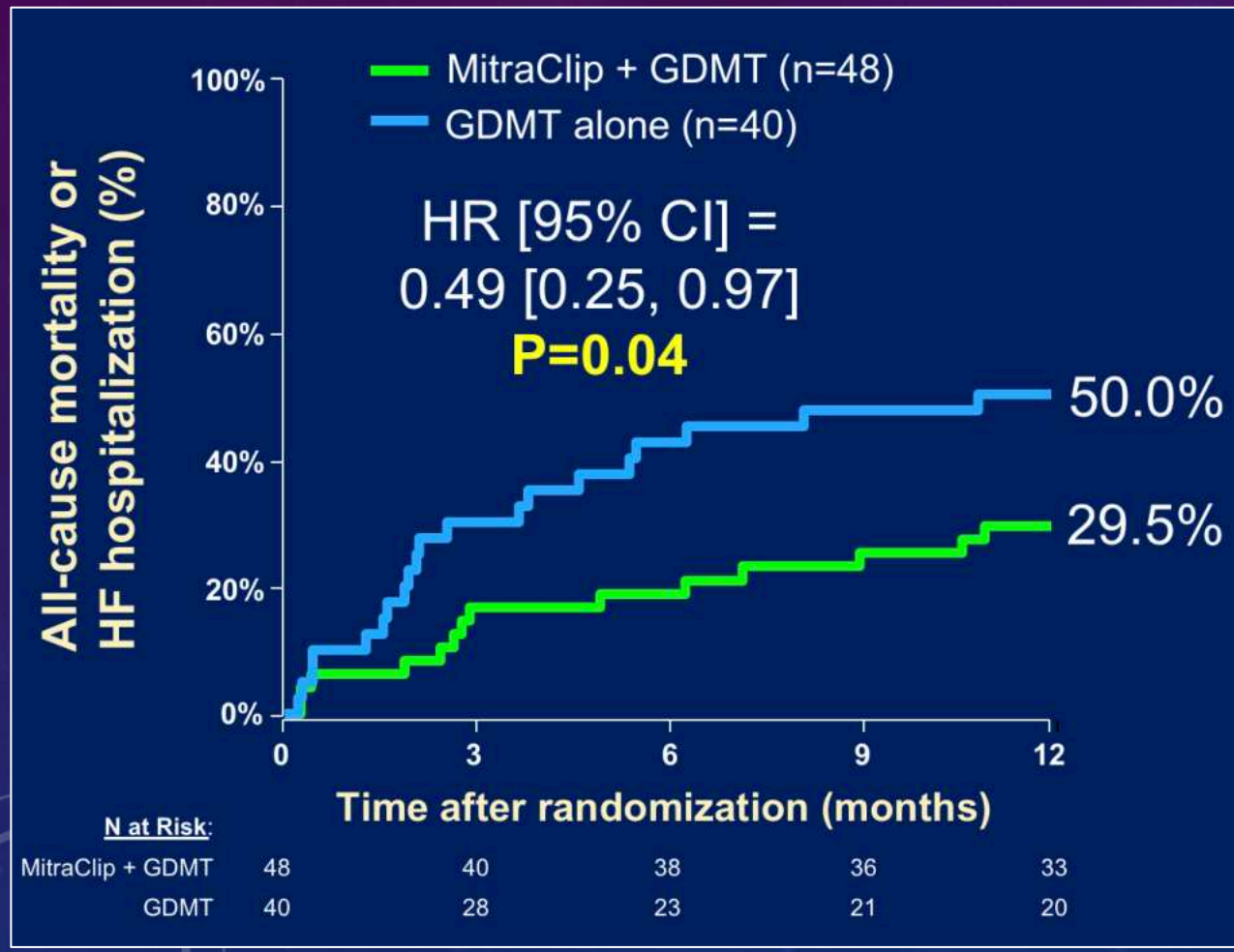


LVEDVI ≤96 ml/m^2 (N=92; 16.8%)

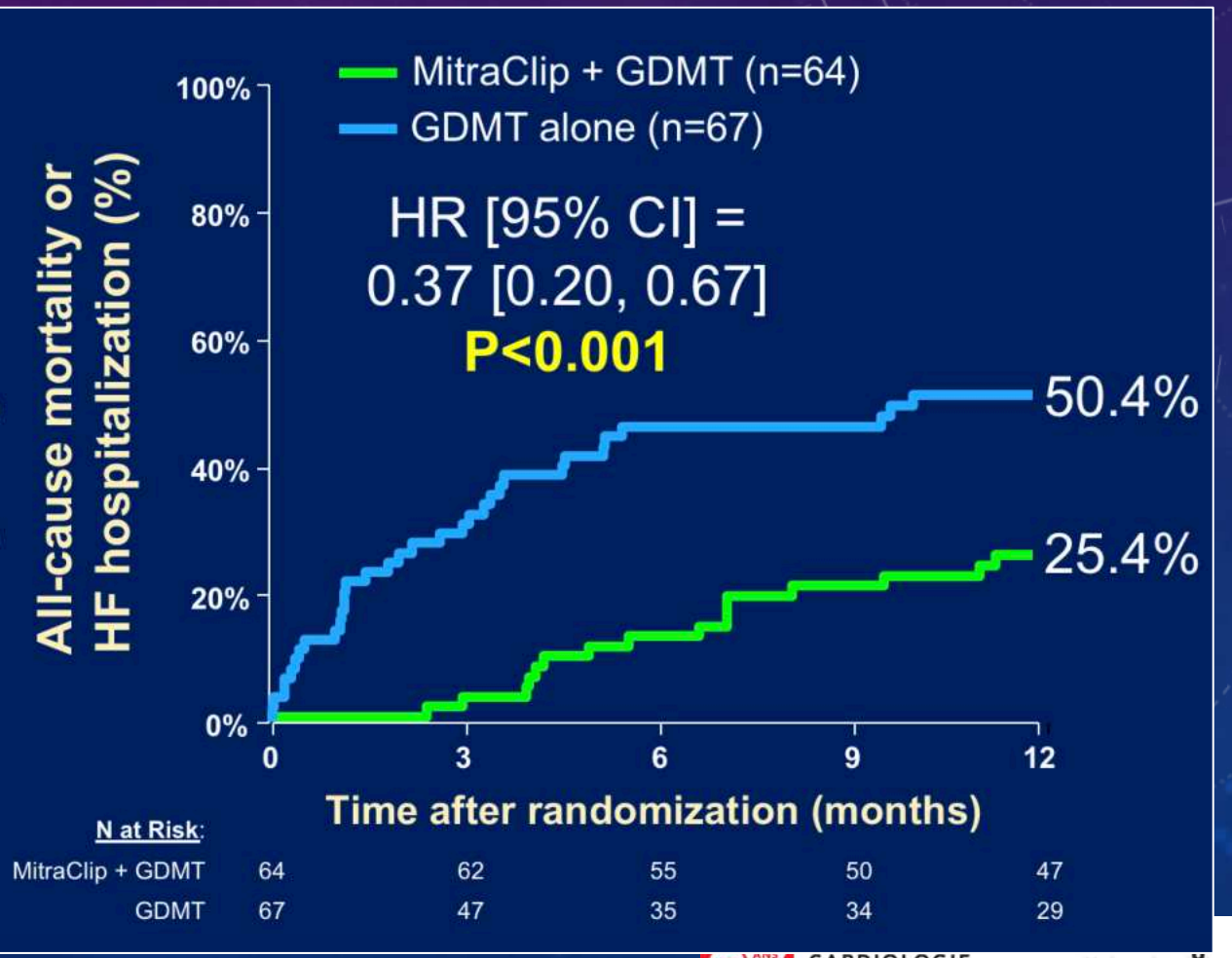


IMPACT OF EROA AND LVEDV: EROA >30-40 MM^2
ALL-CAUSE MORTALITY OR HF HOSPITALIZATION THROUGH 12 MONTHS

LVEDVI >96 ml/m^2 (N=88; 16.1%)

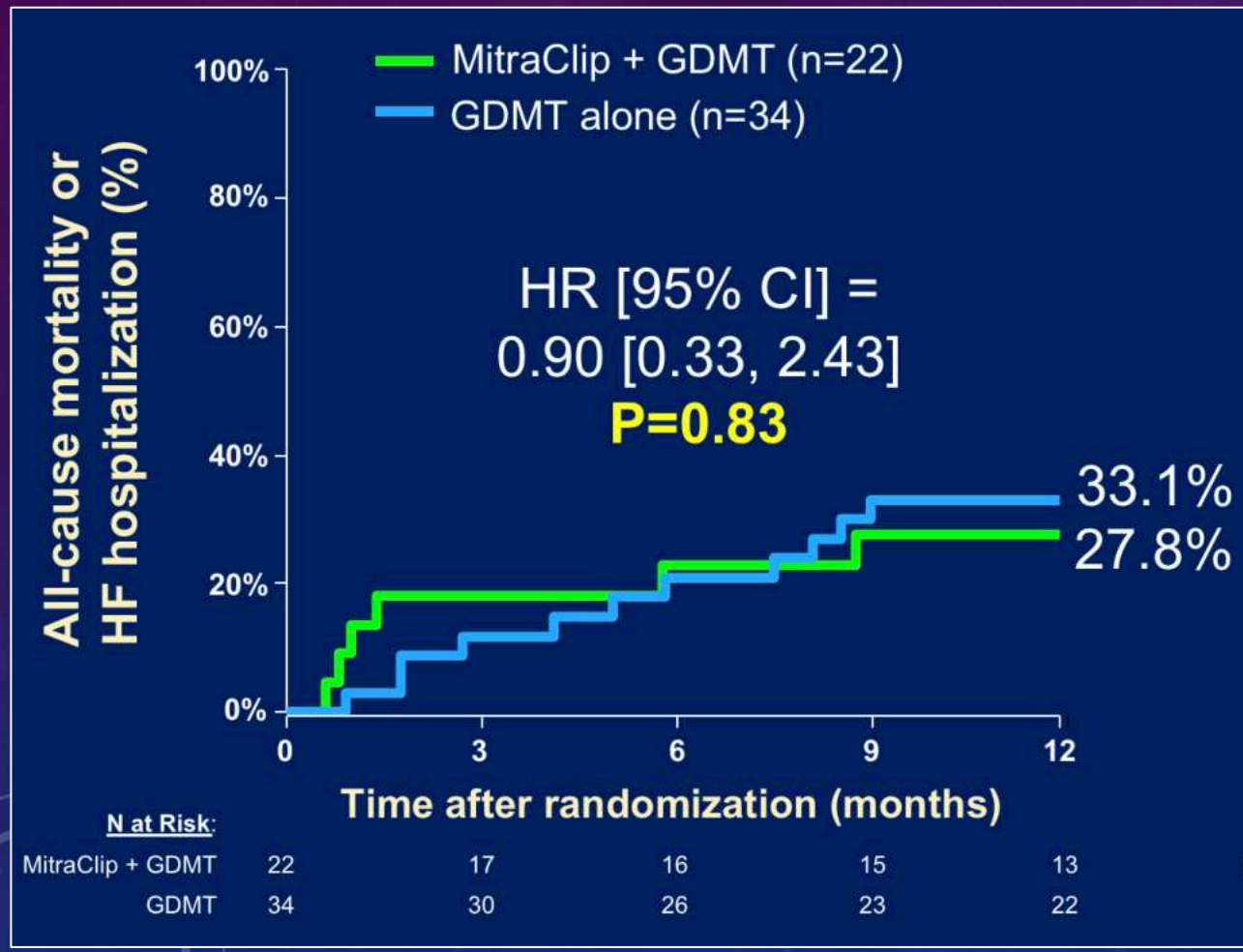


LVEDVI ≤96 ml/m^2 (N=131; 23.9%)

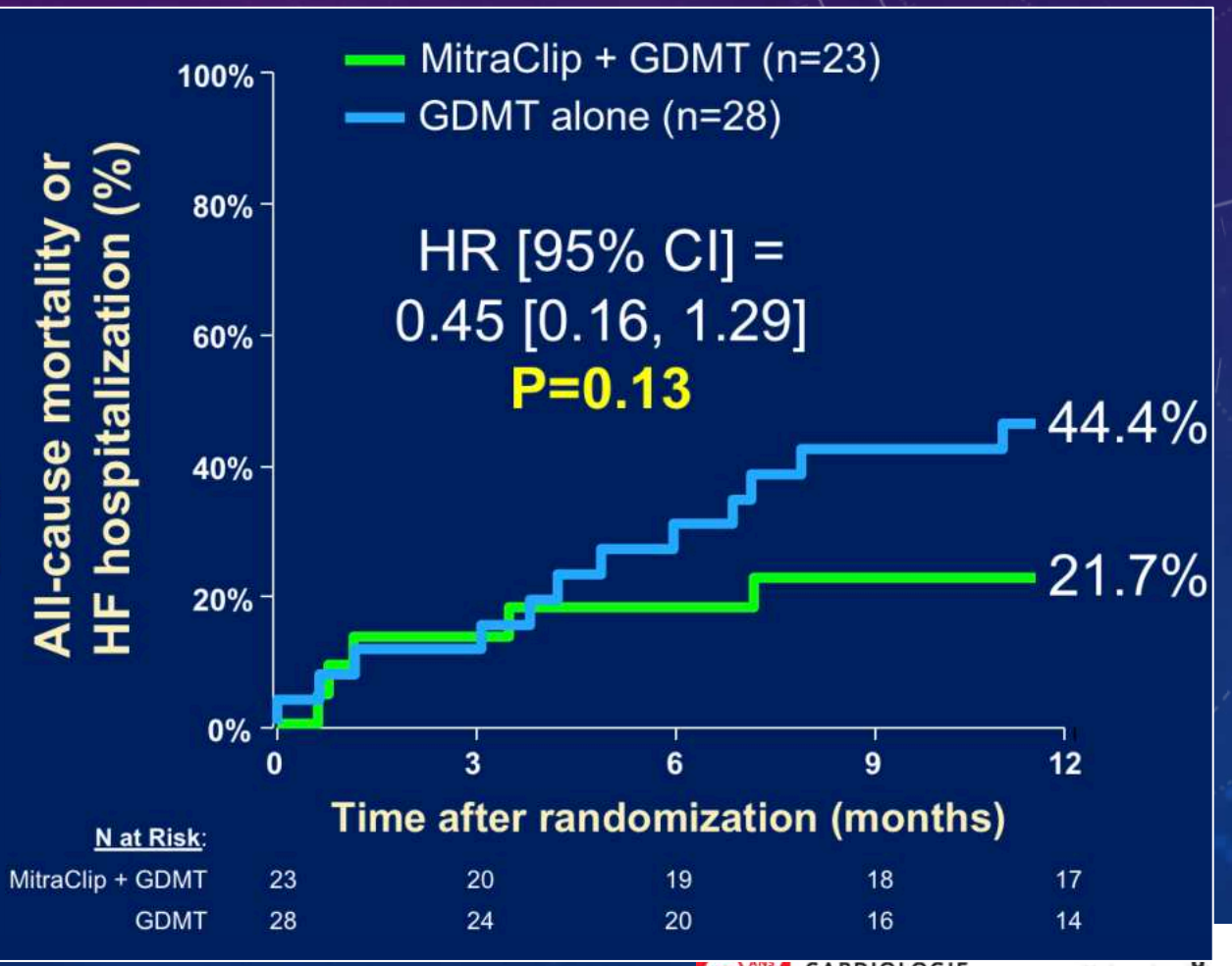


IMPACT OF EROA AND LVEDV: EROA ≤30 MM^2
ALL-CAUSE MORTALITY OR HF HOSPITALIZATION THROUGH 12 MONTHS

LVEDVI >96 ml/m^2 (N=56; 10.2%)



LVEDVI ≤96 ml/m^2 (N=51; 9.3%)



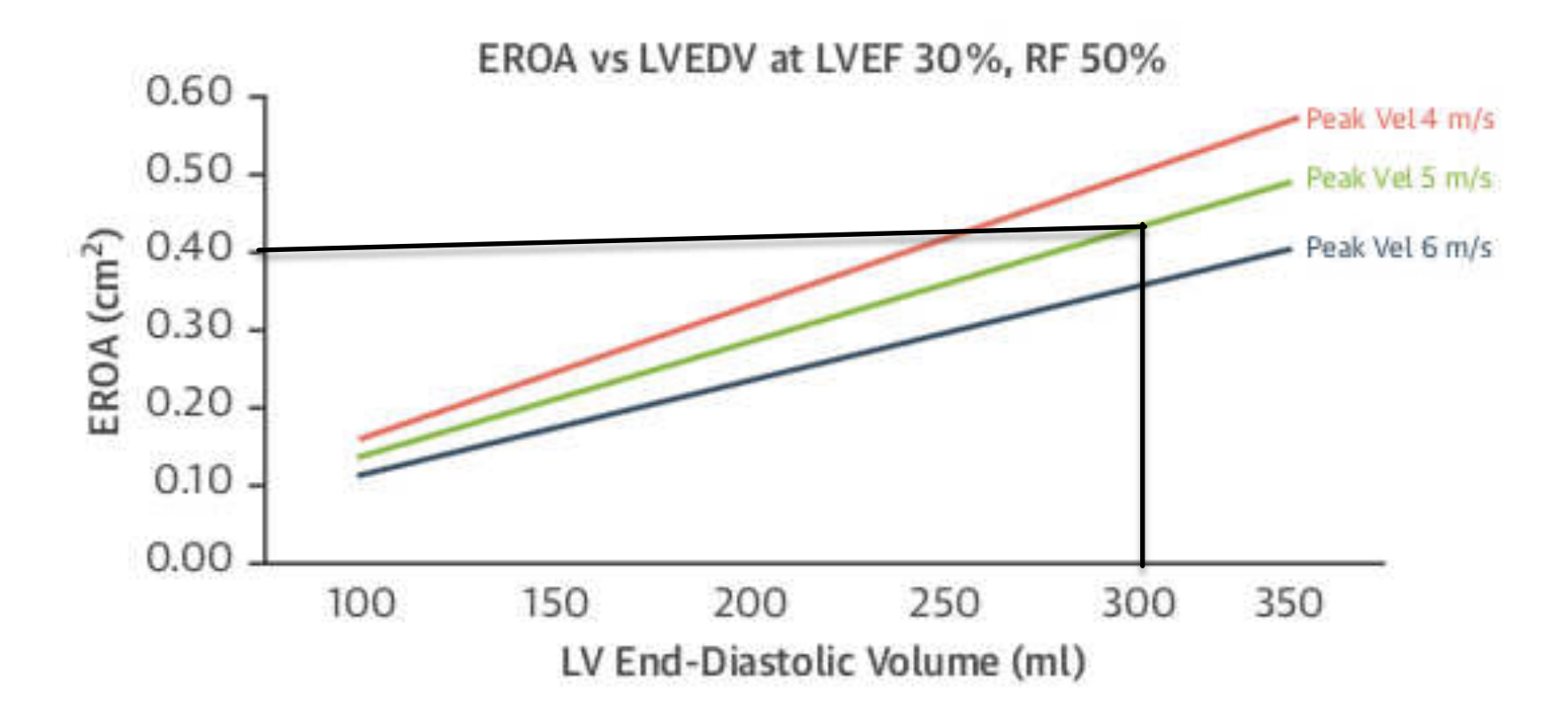
Secondary Mitral Regurgitation

MITRA-FR VS. COAPT

- KEY MESSAGES:
  - Populations were different (very dilated LV vs. less dilated)
  - ***MR Severity was different*** (moderate MR vs. severe MR)
  - ***Aggressive medical therapy titration*** was utilized in COAPT with no significant differences in medical therapy between groups
  - There was ***greater MR reduction*** in COAPT, 95% vs 83% with 2+ or less residual MR
  - Clinical benefit was seen in those patients with severe MR and dilated LV but not end-stage severe dilatation
  - In those patients with end-stage LV dilatation, treatment of moderate MR does not provide benefit (? Too late)

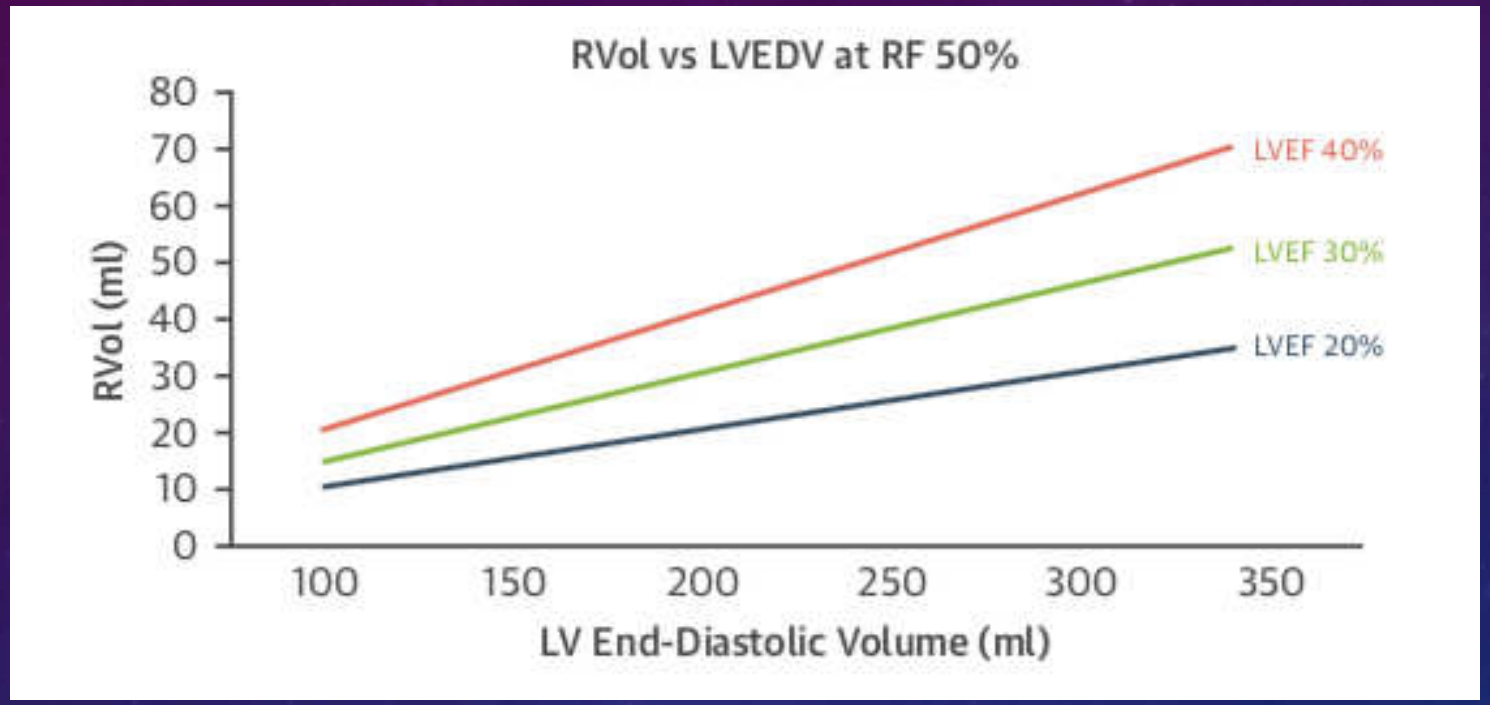
Disproportionate vs. Proportionate MR

Disproportionate vs. Proportionate MR



- For any given regurgitant fraction, the EROA is dependent on both the left ventricular end-diastolic volume (LVEDV) and the left ventricular ejection fraction (LVEF)

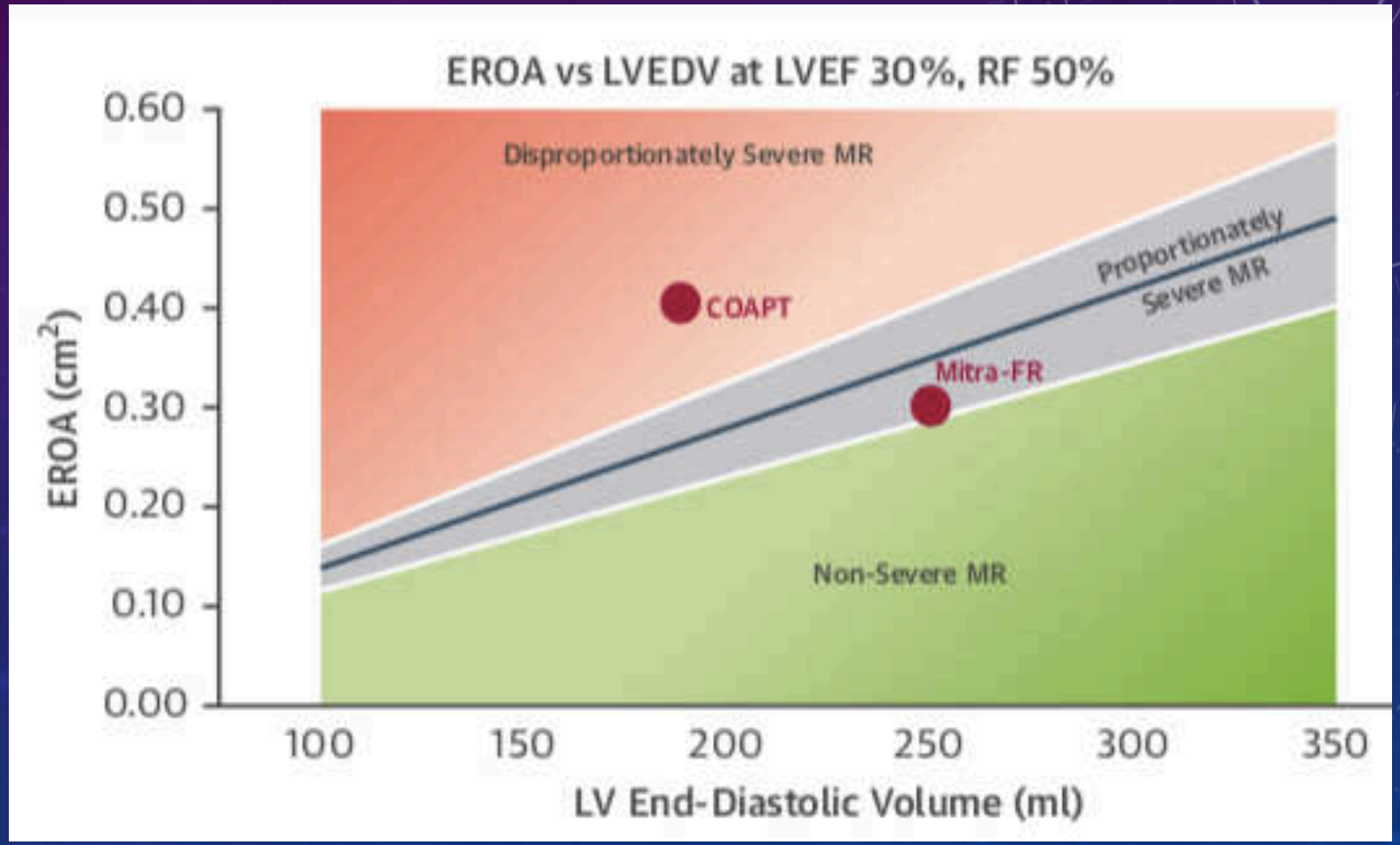
Disproportionate vs. Proportionate MR



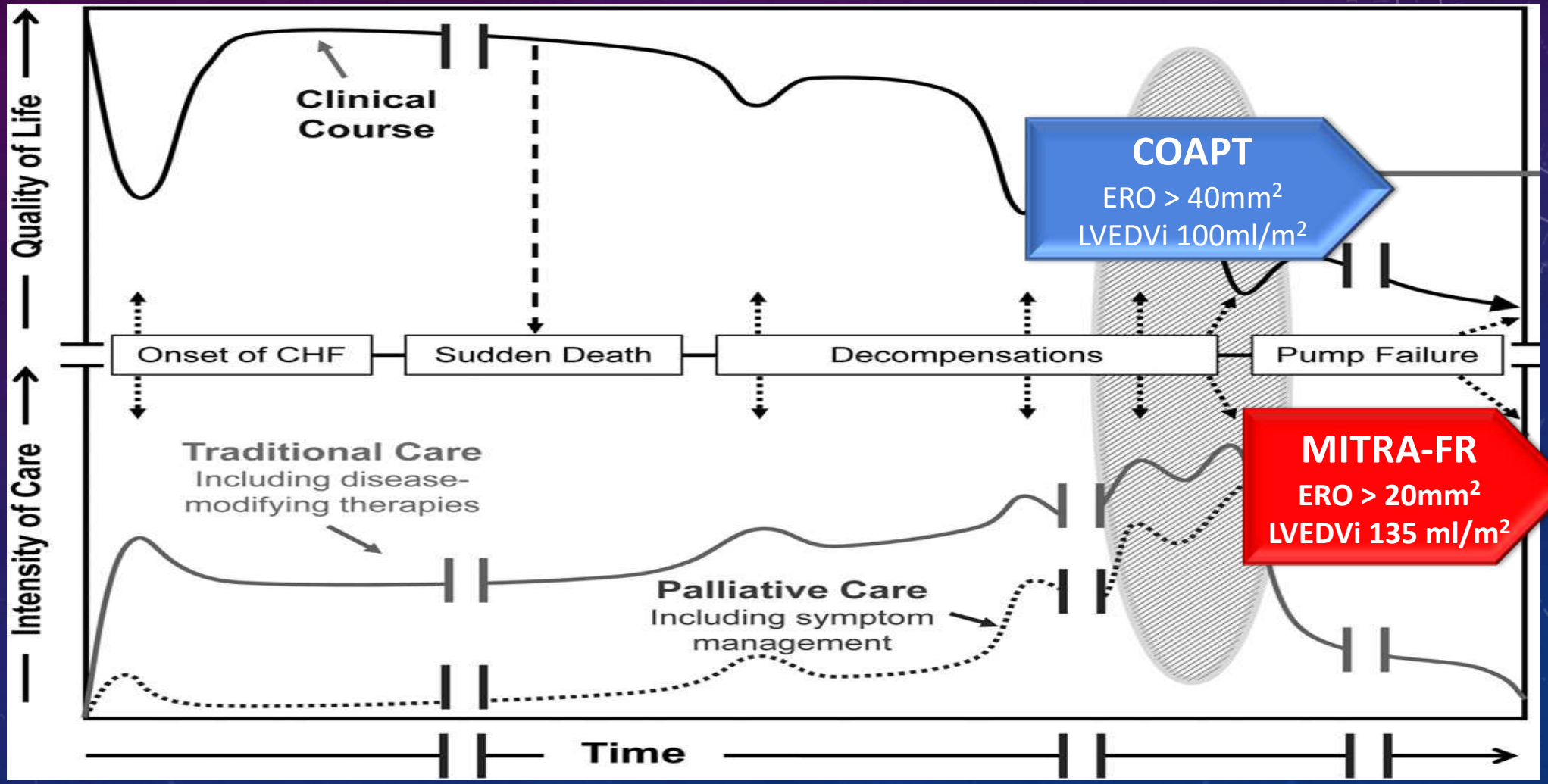
- Regurgitant volume is very dependant on LVEF in the setting of severe MR (RF 50%)
- When the LVEDV is 220 to 250 ml, severe MR (defined by a regurgitant fraction of 50%) corresponds to a regurgitant volume of 45 ml when the LVEF is 40%, 35 ml when the LVEF is 30%, and <25 ml when the LVEF is 20%.

Disproportionate vs. Proportionate MR

- COAPT enrolled patients with **disproportionately** severe MR
- MITRA-FR enrolled patients with **proportionately** severe MR
- The totality of available evidence suggests that patients with chronic heart failure respond favorably to transcatheter mitral valve repair IF they exhibit degrees of MR that are disproportionately greater than might be expected from the degree of LV chamber enlargement.

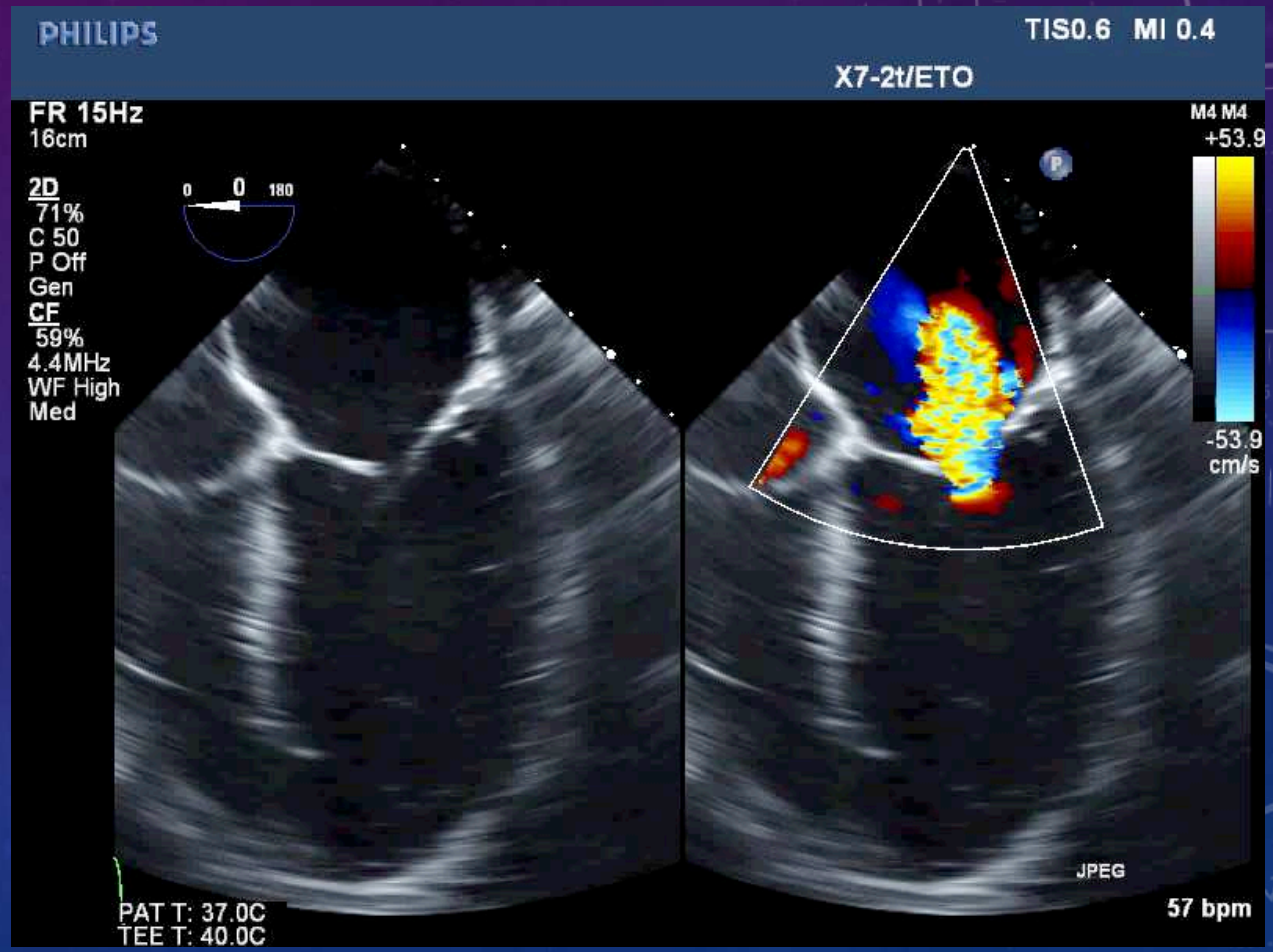


The Spectrum of Secondary MR



Case Presentation

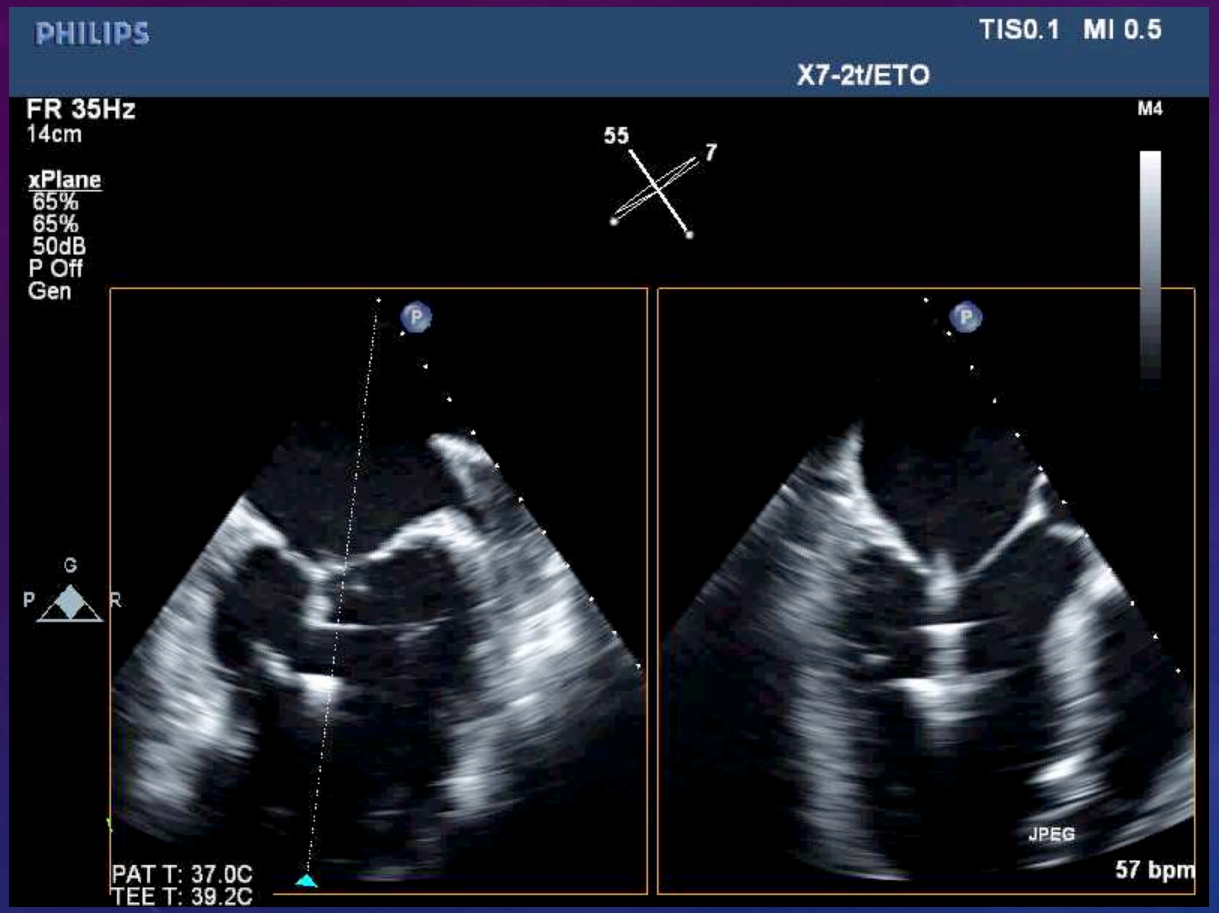
- Twelve months following randomization to ***Medical Therapy in COAPT***:
  - Hospitalized for decompensated heart failure on **18** separate occasions (January 2017-December 2017)
  - Renal function deteriorating, creat 400
  - NYHA IV

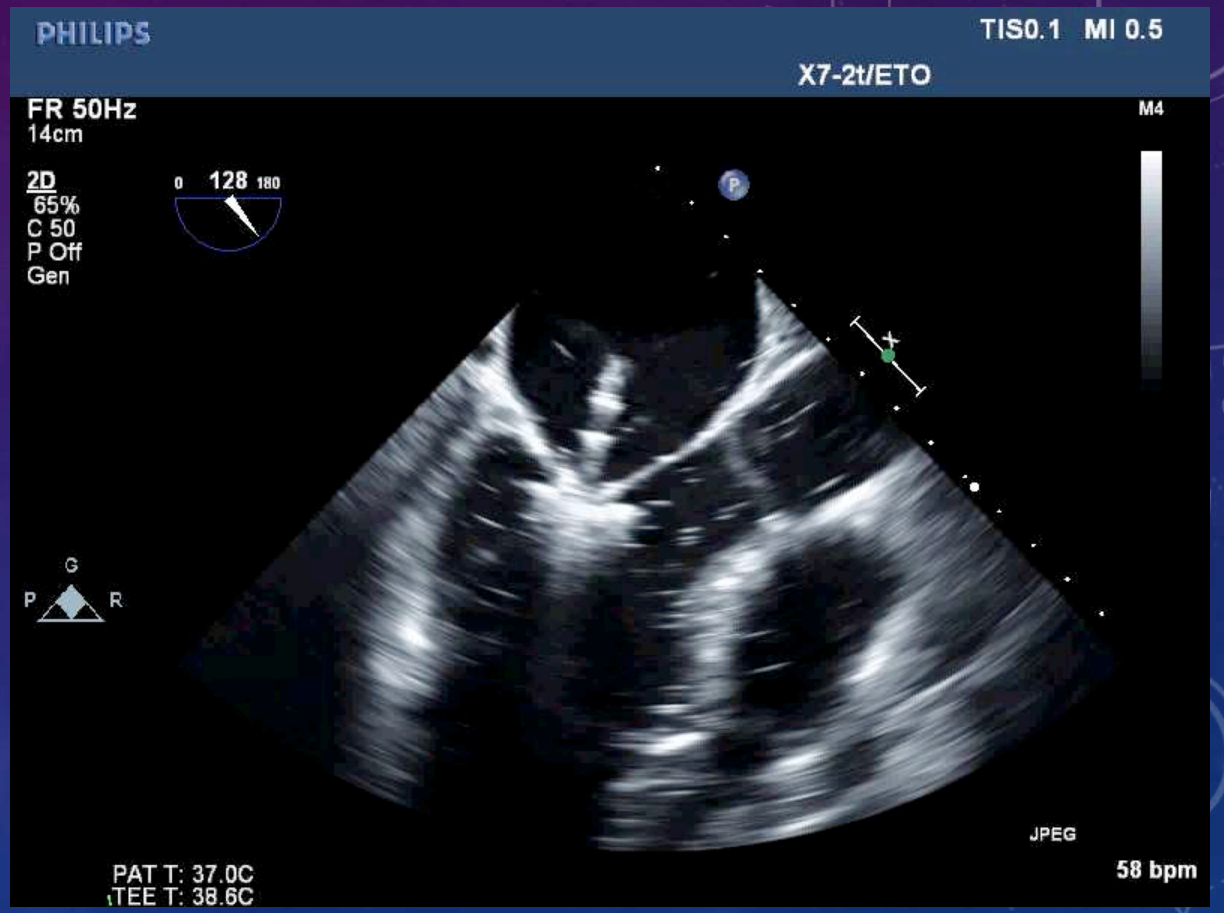


Case Presentation

- Following discussion with the Heart Team and treating physician, decision was made to perform protocol deviation and perform the MitraClip procedure
- COAPT Trial protocol deviation accepted
- Patient electively admitted for MitraClip procedure performed on January 18, 2018

Case Presentation





Case Presentation

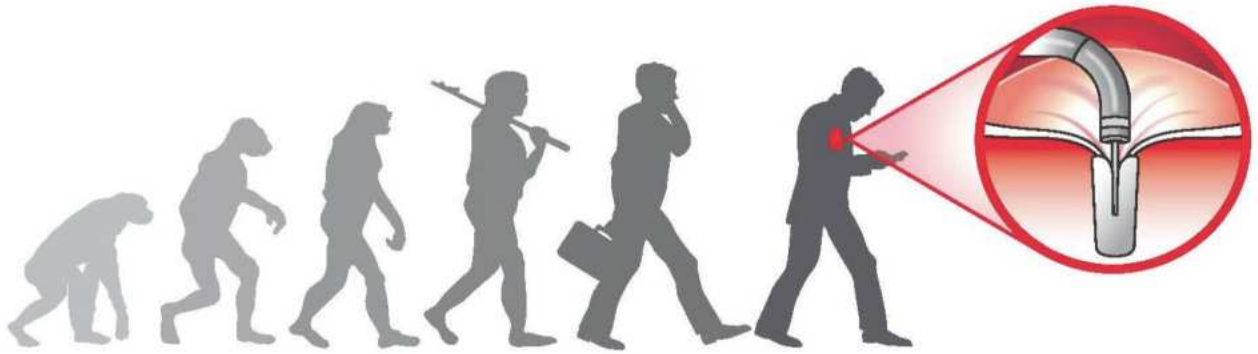
- Follow Up (12 months)
  - Clinic visit **16/12/2018**
  - Patient doing well, walking daily
  - NYHA Class 1-2
  - Echocardiogram:
    - EF 33%
    - MR 1+

- No further admissions for heart failure since January 2018

Who are ideal candidates for MitraClip therapy for FMR?

- Severe symptomatic secondary mitral regurgitation
- Optimally medically treated as per HF Guidelines including device therapy (CRT) as required
- LVEF >20%
- NO evidence of severe end-stage LV dilatation
  - Procedure may be successful but unlikely to change natural history of the disease
- Procedure judged feasible by an experienced MitraClip team

GOAL OF THERAPY: MAXIMAL reduction of MR



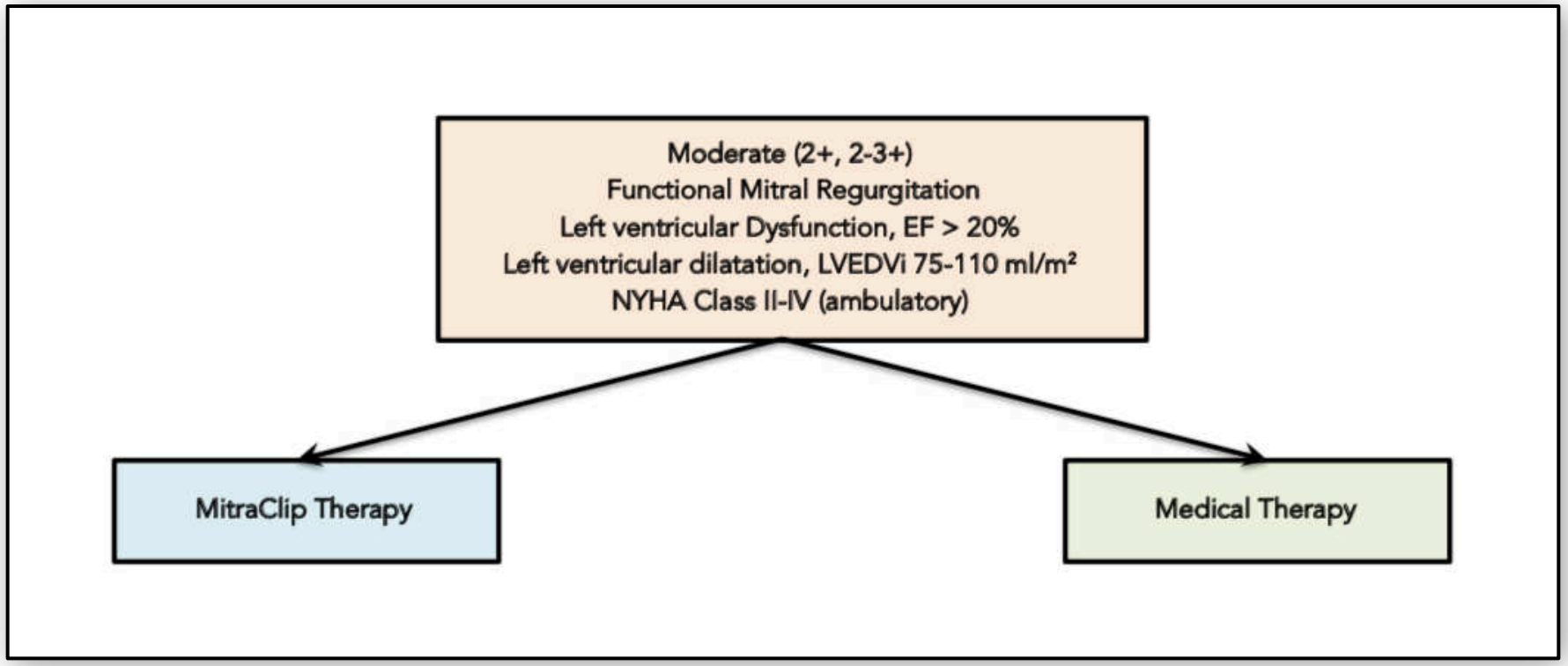
THE EVOLVE-MR TRIAL

EVALUATION OF OUTCOMES OF MITRACLIP FOR THE TREATMENT OF LOW EJECTION FRACTION AND FUNCTIONAL MITRAL VALVE REGURGITATION-MODERATE MR

STUDY DESIGN

THE EVOLVE-MR TRIAL

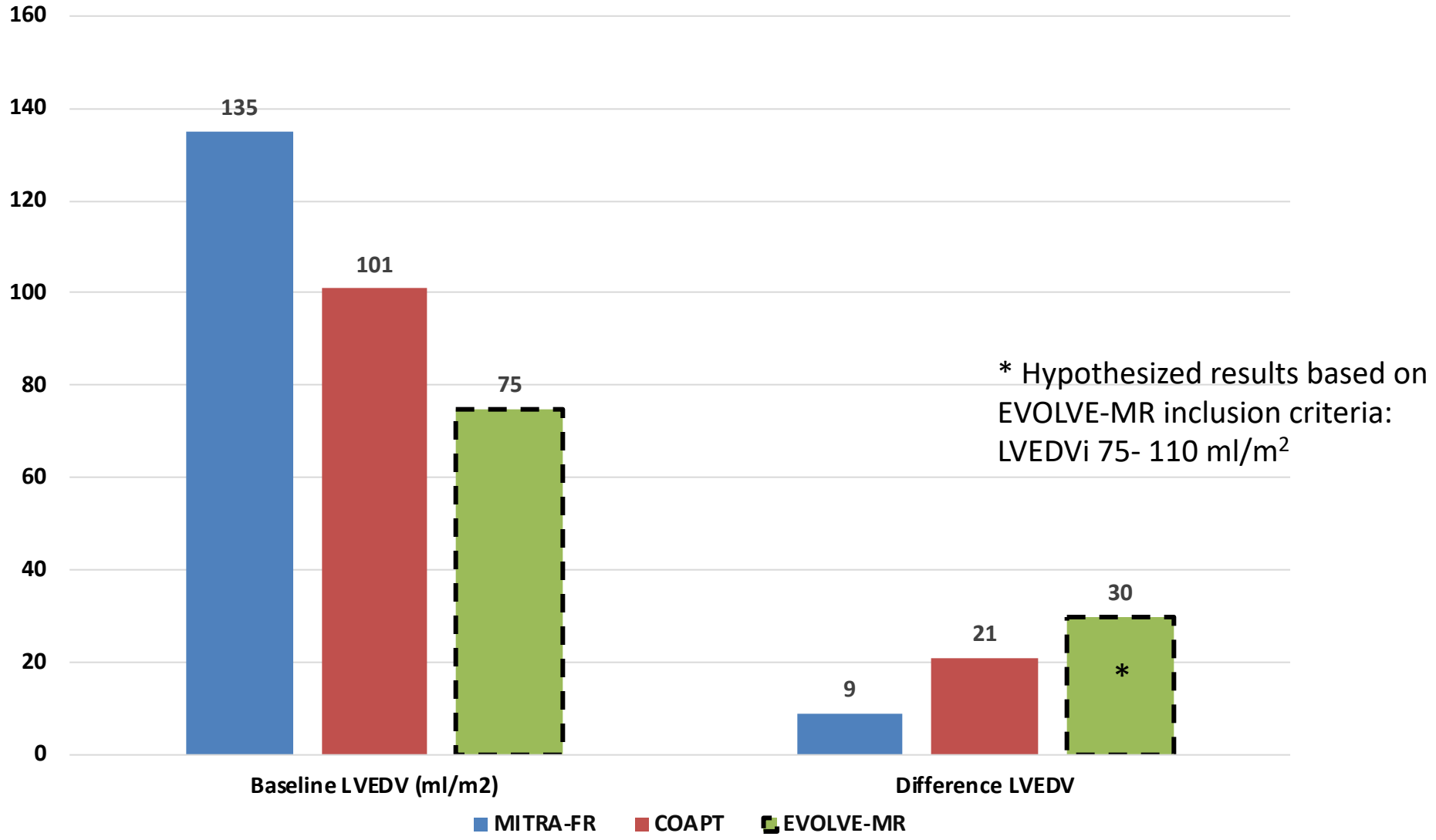
Randomized trial of medical therapy vs. MitraClip in HF patients with MODERATE MR



EVOLVE-MR

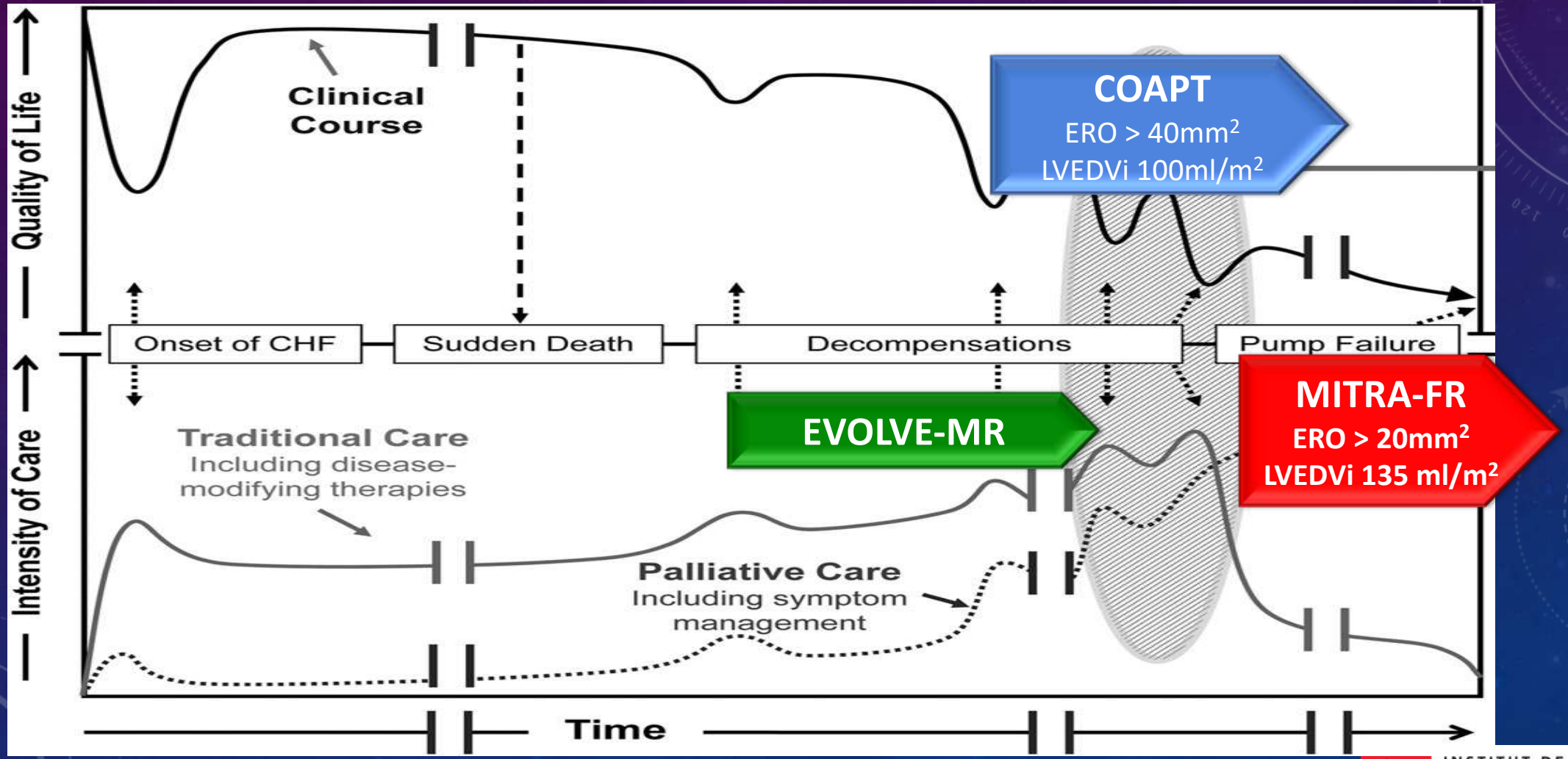
Multicenter trial in Canada that will identify the optimal strategy to treat patients with **Heart Failure** and **Moderate** Mitral Regurgitation to improve left ventricular remodelling and the quality of life

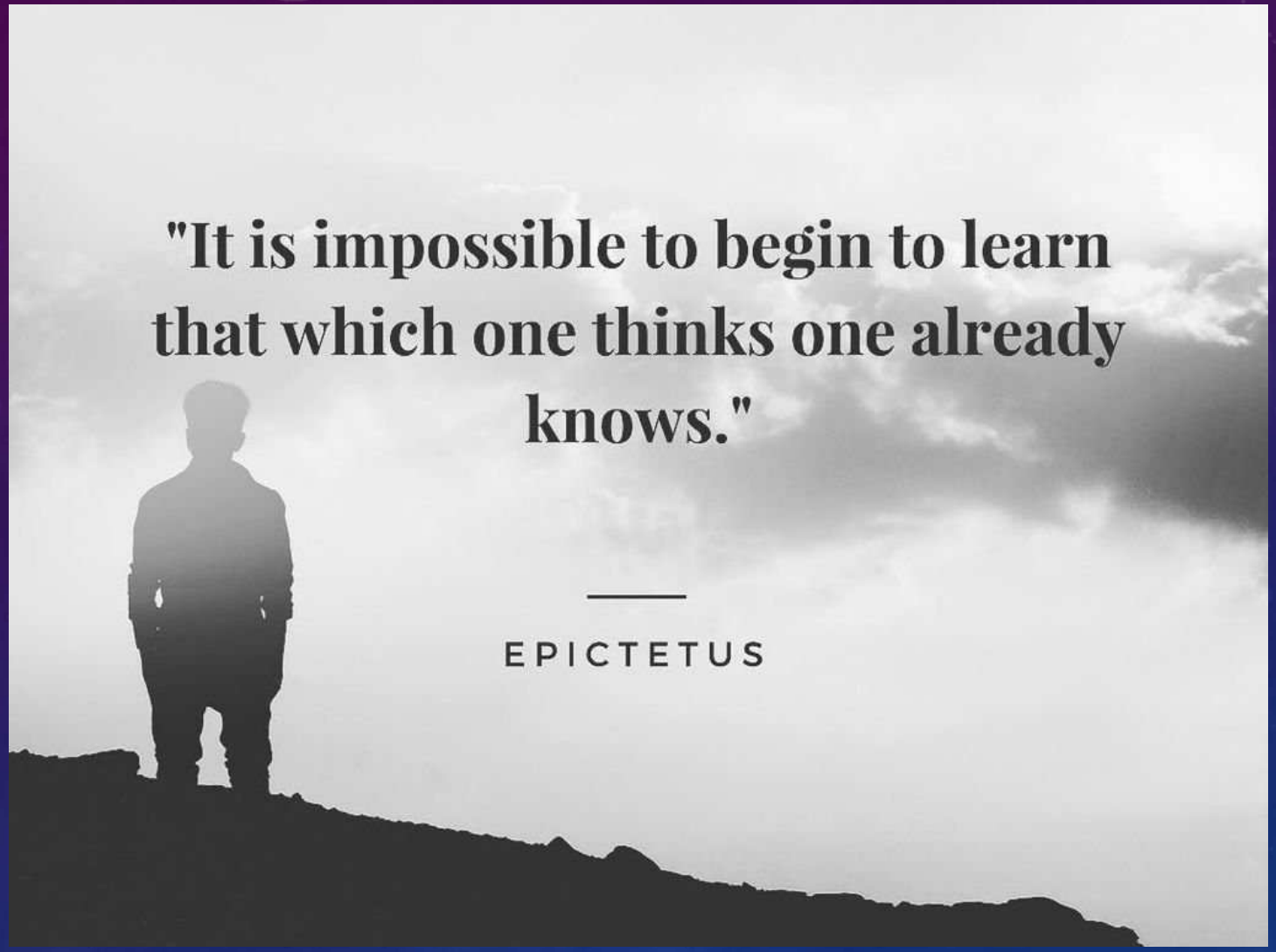
LV Remodelling in RCT of MitraClip



* Hypothesized results based on EVOLVE-MR inclusion criteria: LVEDVi 75- 110 ml/m^2

Should we intervene earlier for Moderate Secondary MR?





THANK YOU FOR YOUR ATTENTION