Riparazione della valvola mitrale: Cosa abbiamo imparato e cosa ci aspettiamo

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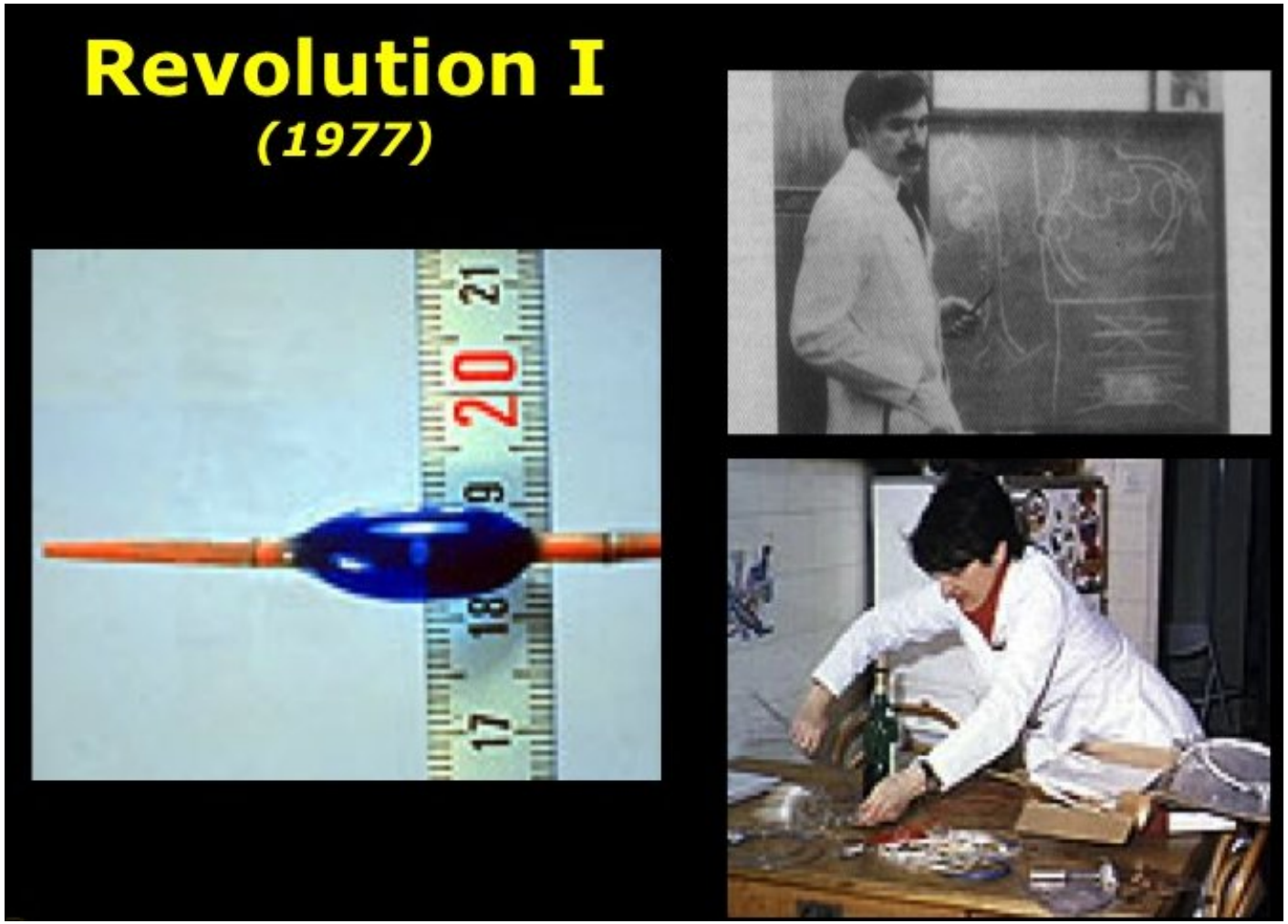
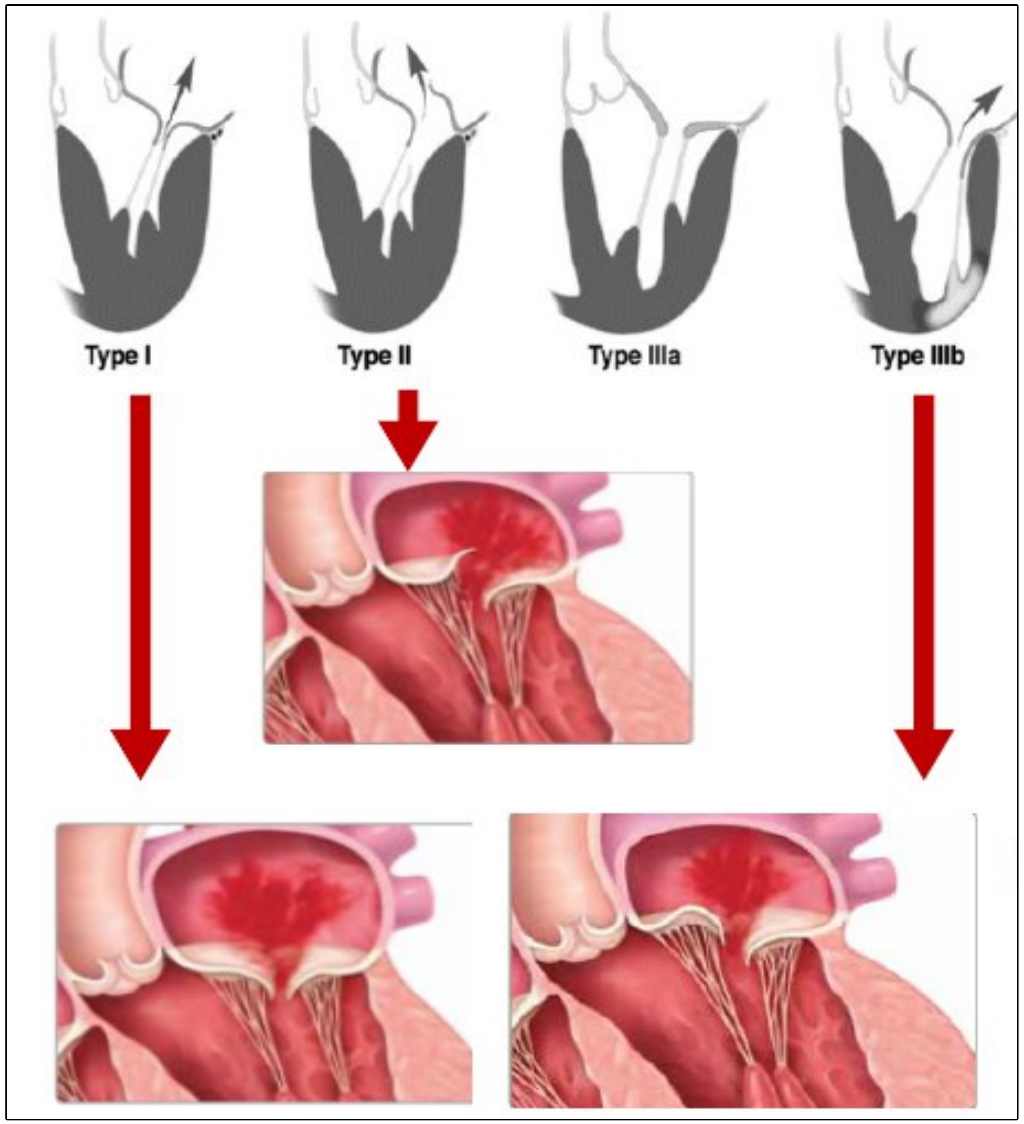
Università degli Studi della Campania
A.O.Monaldi-Ospedale dei Colli

Once upon a time, 40 years ago…



MR: Etiology



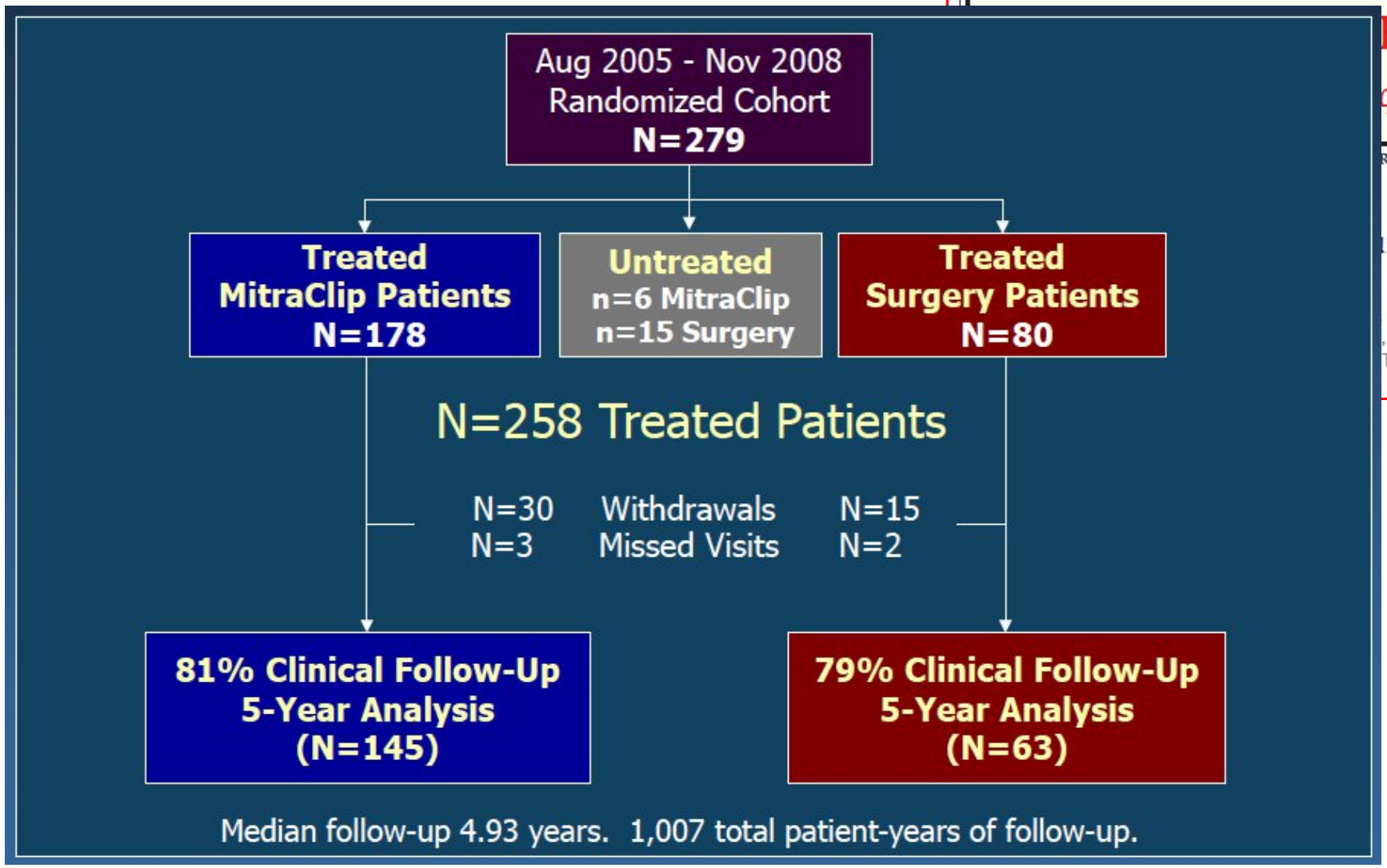
Degenerative

Degenerative disease of MV apparatus

Functional

Regional or global remodeling of LV w/o MV abnormalities

EVEREST II Study



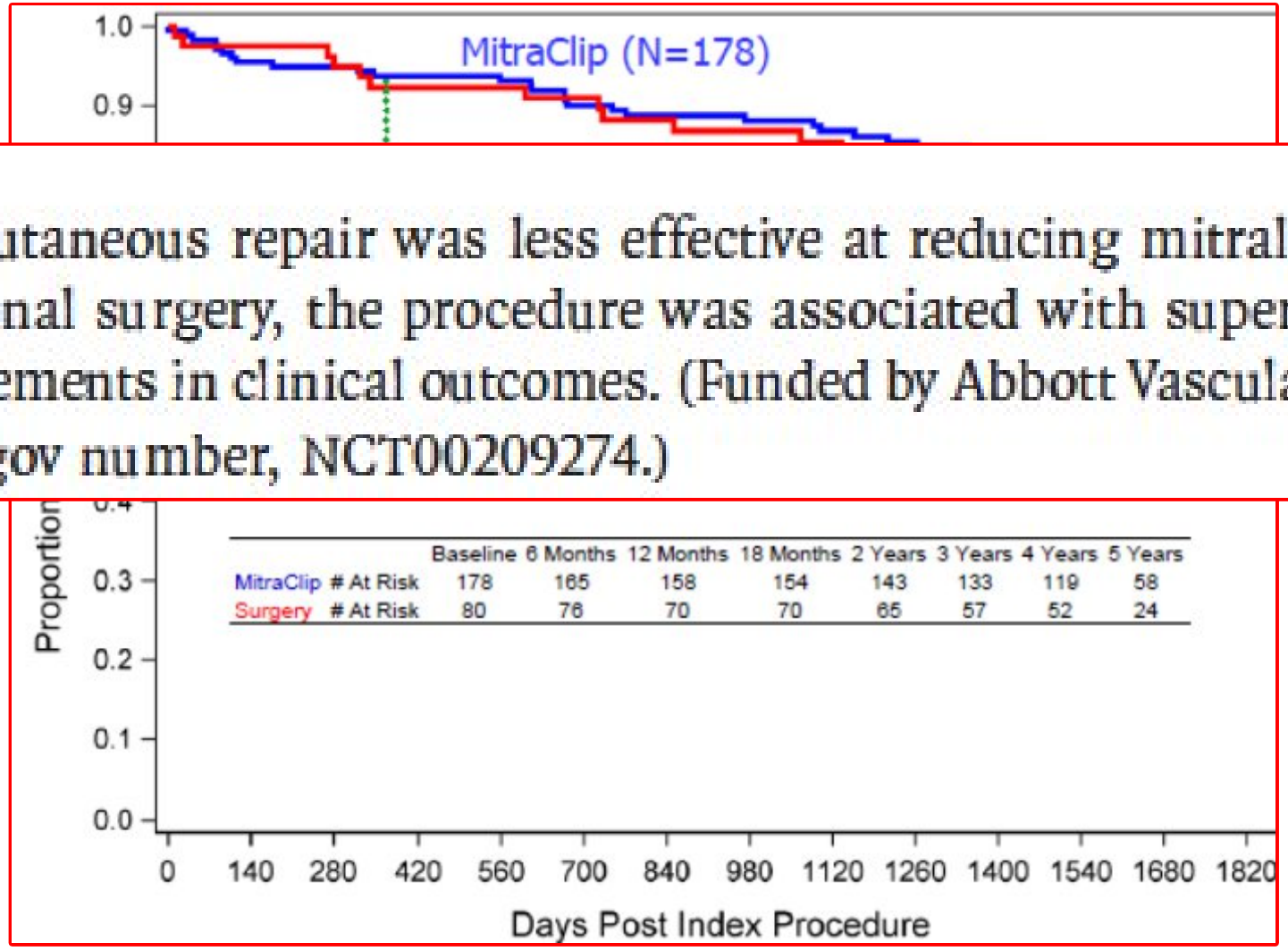

ENGLAND
of MEDICINE

RIL 14, 2011 VOL. 364 NO. 15

rgery for Mitral Regurgitation

Glower, M.D., Saibal Kar, M.D., Michael J. Rinaldi, M.D.,
, Ph.D., Robert Siegel, M.D., Geoffrey A. Rose, M.D.,
Trento, M.D., Eric R. Skipper, M.D., Tommy Fudge, M.D.,
and Laura Mauri, M.D., for the EVEREST II Investigators*

5-Years FU Survival Rate



CONCLUSIONS

Although percutaneous repair was less effective at reducing mitral regurgitation than conventional surgery, the procedure was associated with superior safety and similar improvements in clinical outcomes. (Funded by Abbott Vascular; EVEREST II ClinicalTrials.gov number, NCT00209274.)

2013: MitraClip received FDA approval for DMR

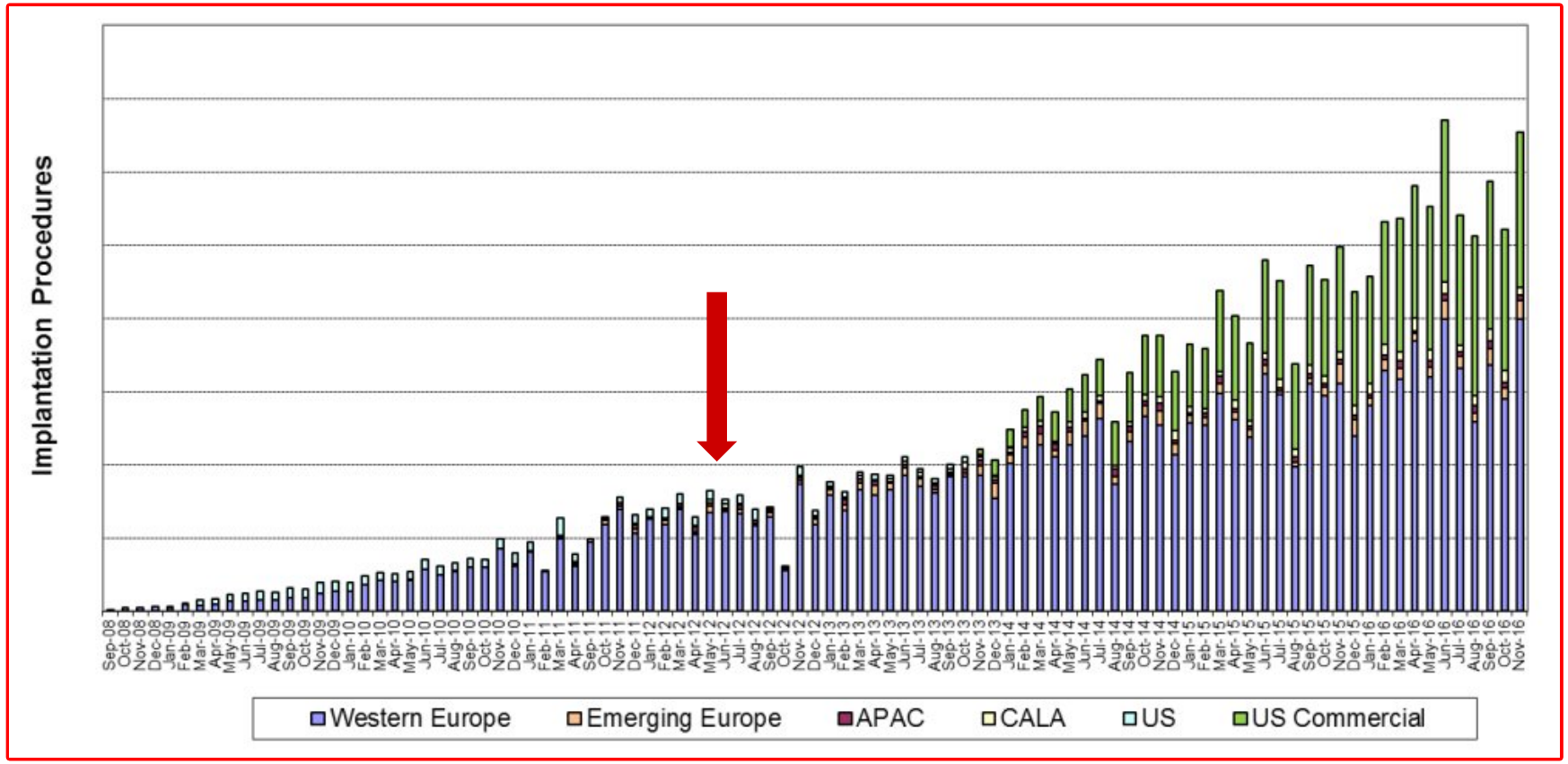
The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 APRIL 14, 2011 VOL. 364 NO. 15

Percutaneous Repair or Surgery for Mitral Regurgitation

Ted Feldman, M.D., Elyse Foster, M.D., Donald D. Glower, M.D., Saibal Kar, M.D., Michael J. Rinaldi, M.D., Peter S. Fail, M.D., Richard W. Smalling, M.D., Ph.D., Robert Siegel, M.D., Geoffrey A. Rose, M.D., Eric Engeron, M.D., Catalin Loghin, M.D., Alfredo Trento, M.D., Eric R. Skipper, M.D., Tommy Fudge, M.D., George V. Letsou, M.D., Joseph M. Massaro, Ph.D., and Laura Mauri, M.D., for the EVEREST II Investigators*

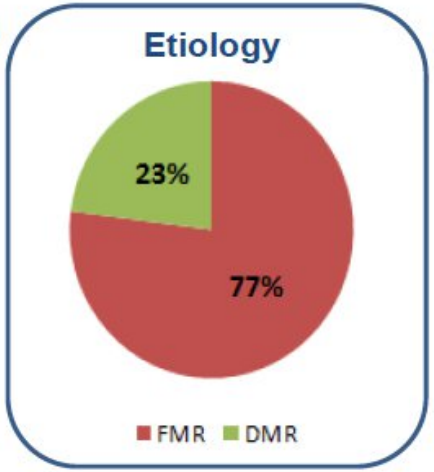
Left ventricular ejection fraction — %	60.0±10.1	60.6±11.0
Cause of mitral regurgitation — no. (%)		
Functional	49 (27)	26 (27)
Degenerative	73%	73%
With anterior or bileaflet flail or prolapse	58 (32)	25 (26)
With posterior flail or prolapse	72 (39)	42 (44)
With no flail and no prolapse	5 (3)	2 (2)

Global MitraClip Experience



EU Registries in the Real Word: Etiology

Access EU
N = 487



SENTINEL
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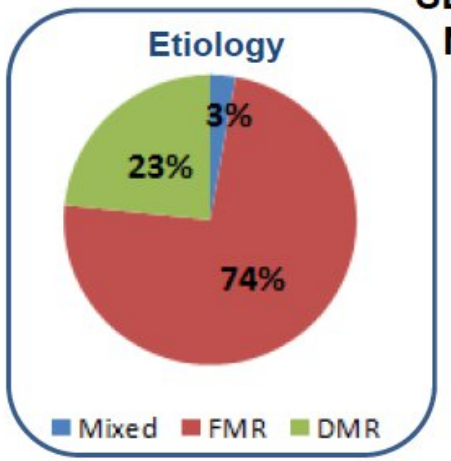
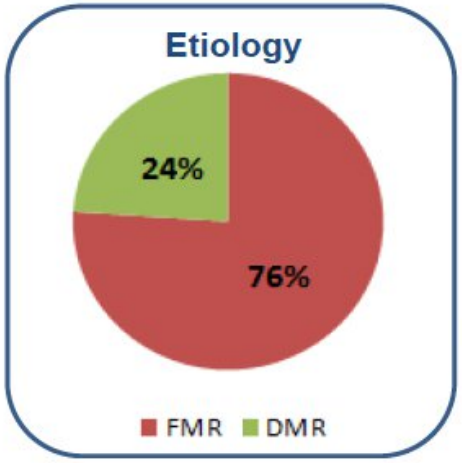
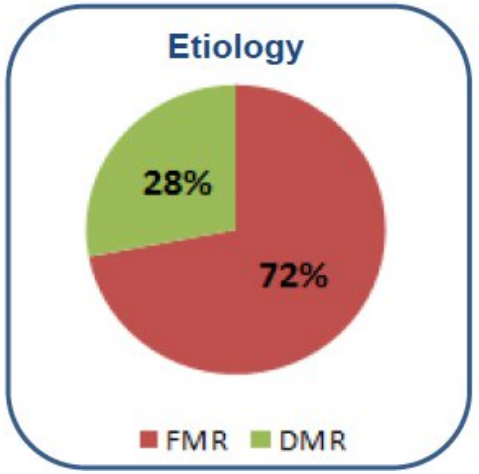


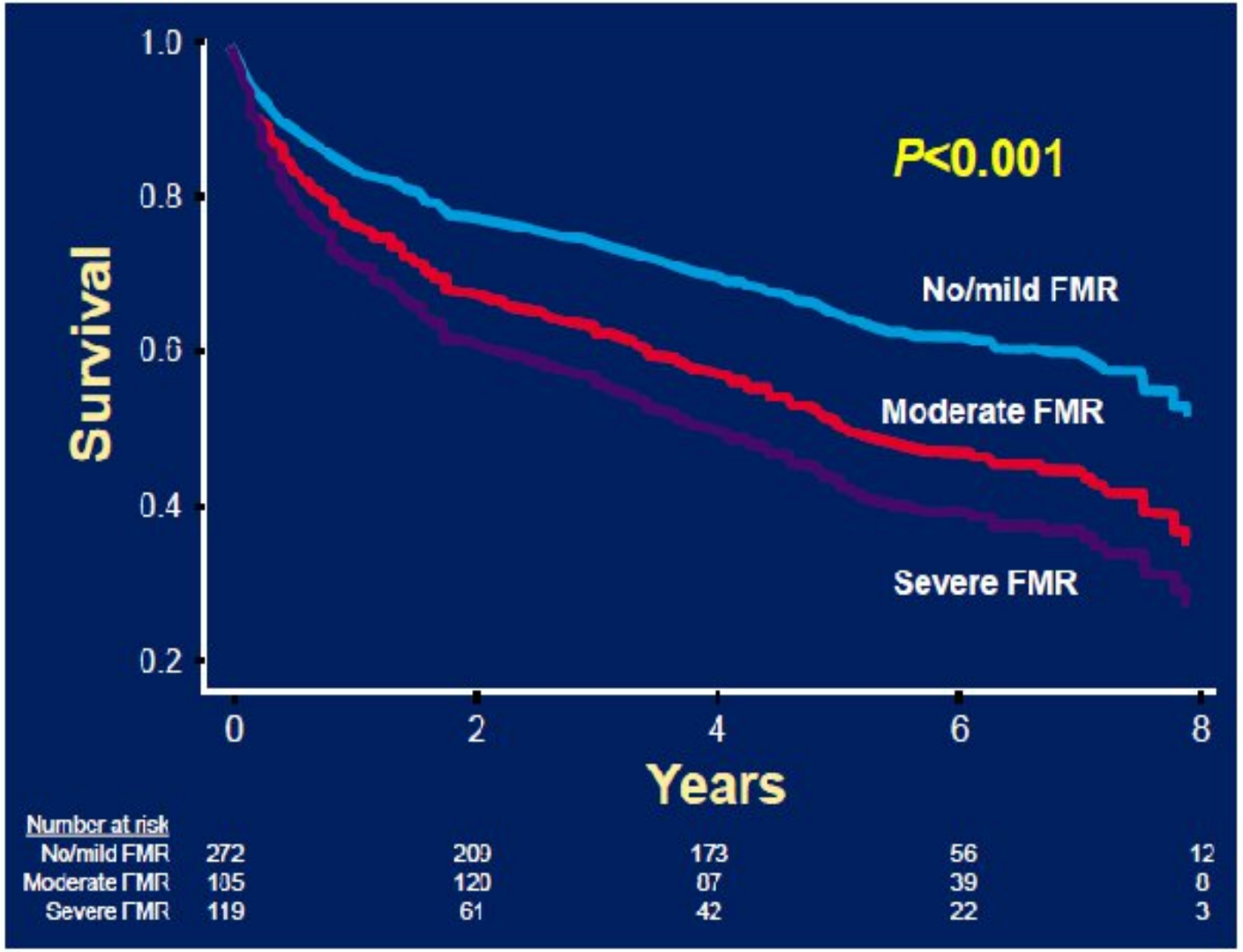


Grasp-IT
N = 304

TRAMI
N = 1064



Impact of FMR on HFrEF Patients



- Prospective study of 576 pts with HFrEF
- 47% died during median 5-year FU
  - severe FMR in 21%
  - mod FMR in 32%

- Severe secondary MR is an independent predictor of long-term mortality after multivariable adjustment for clinical, echo, biomarker and medication variables

Goliasch G et al. *EHJ* 2018;39:39-46

Is Mitraclip Effective in Treating FMR?

Two RCTs Reported Primary Results in 2018 evaluating MitraClip + GDMT against GDMT alone

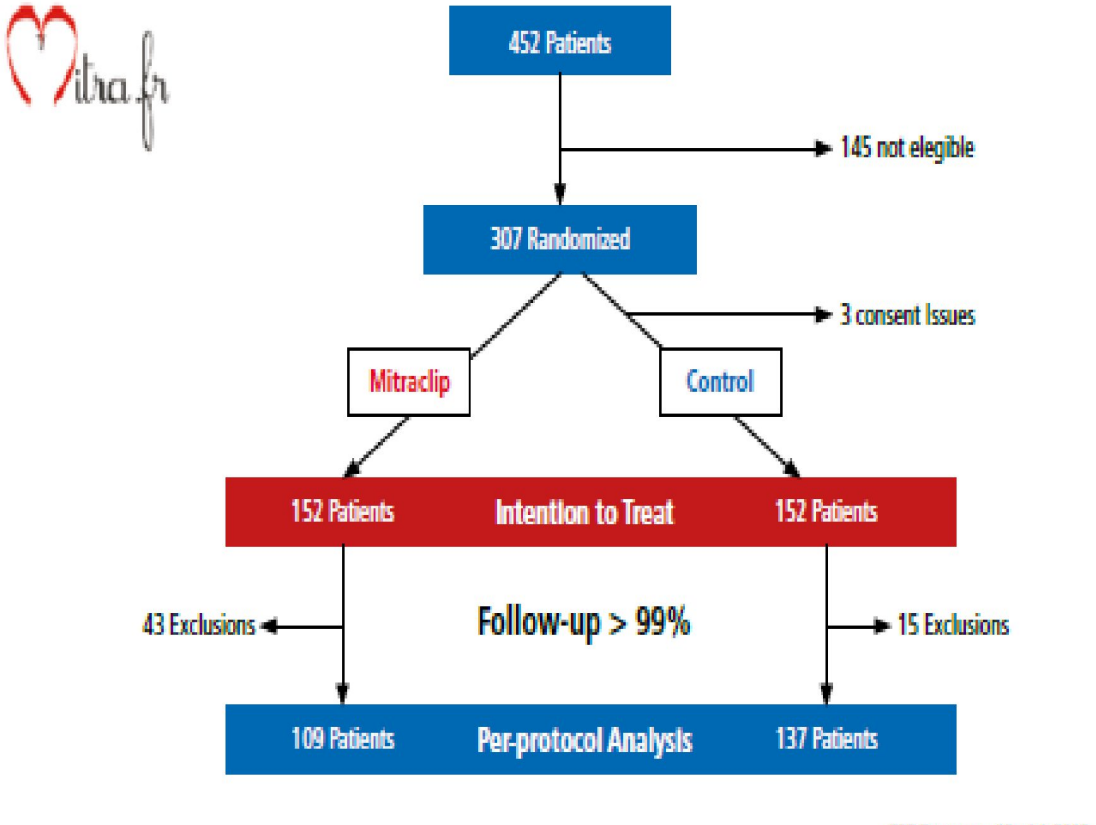
Mitra-FR

- Sponsored by Investigators and funded by French Ministry of Health
- MR severity defined per European guidelines
- published in NEJM.org

COAPT

- Sponsored by Abbott and designed in partnership with FDA and study PI's to seek an FMR indication approval
- MR severity defined per ACC/ASE guidelines
- published in NEJM.org

MITRA-FR – Trial Design

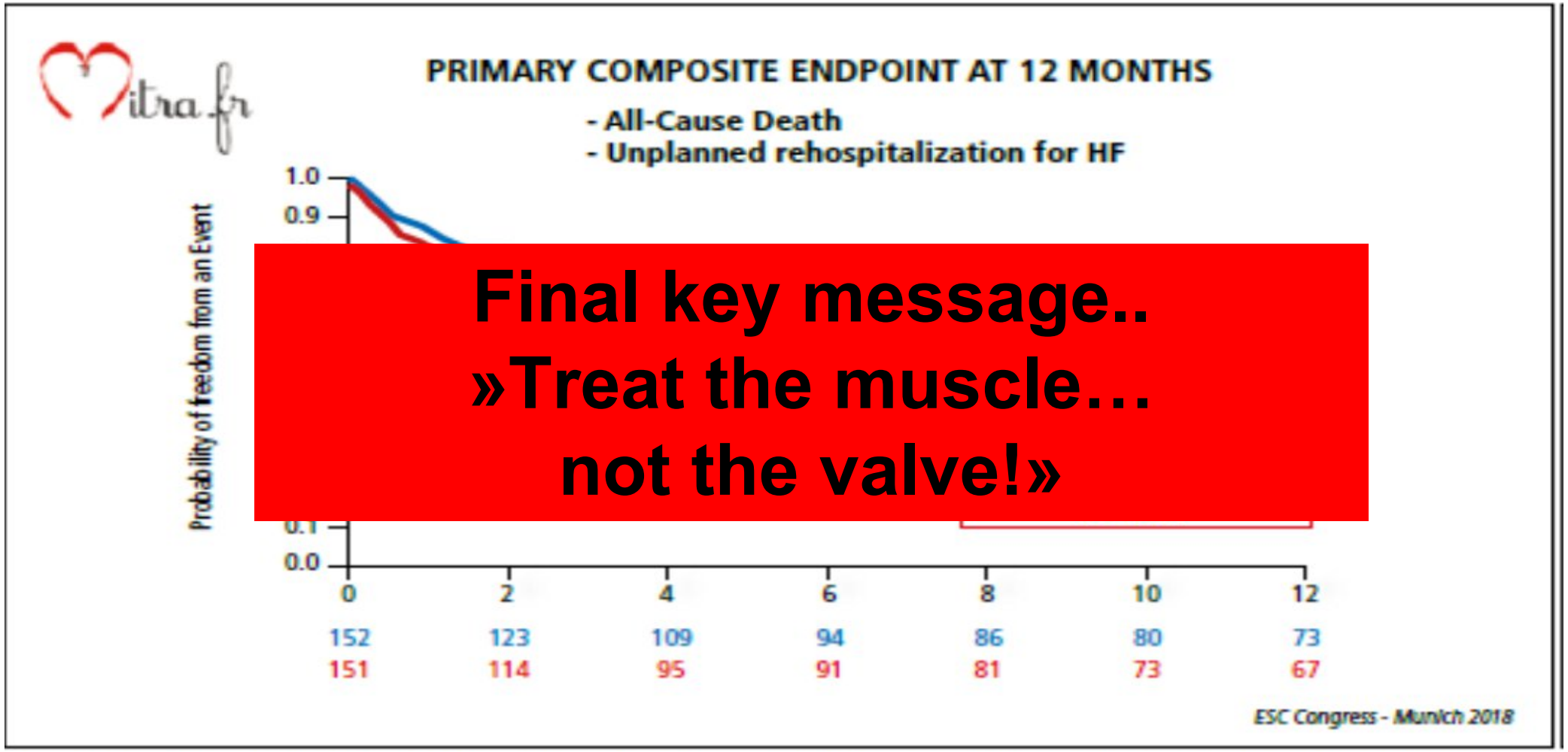


Inclusion Criteria

- Symptomatic despite Optimal Treatment (NYHA ≥II).
- At least one hospitalization for HF within 12 months preceding randomization
- Severe Secondary MR → ERO > 20 mm² or R.vol>30 mL/beat
- 15% < EF < 40%
- Not eligible for surgery "Heart Team"
- Centralized echocardiographic Corelab

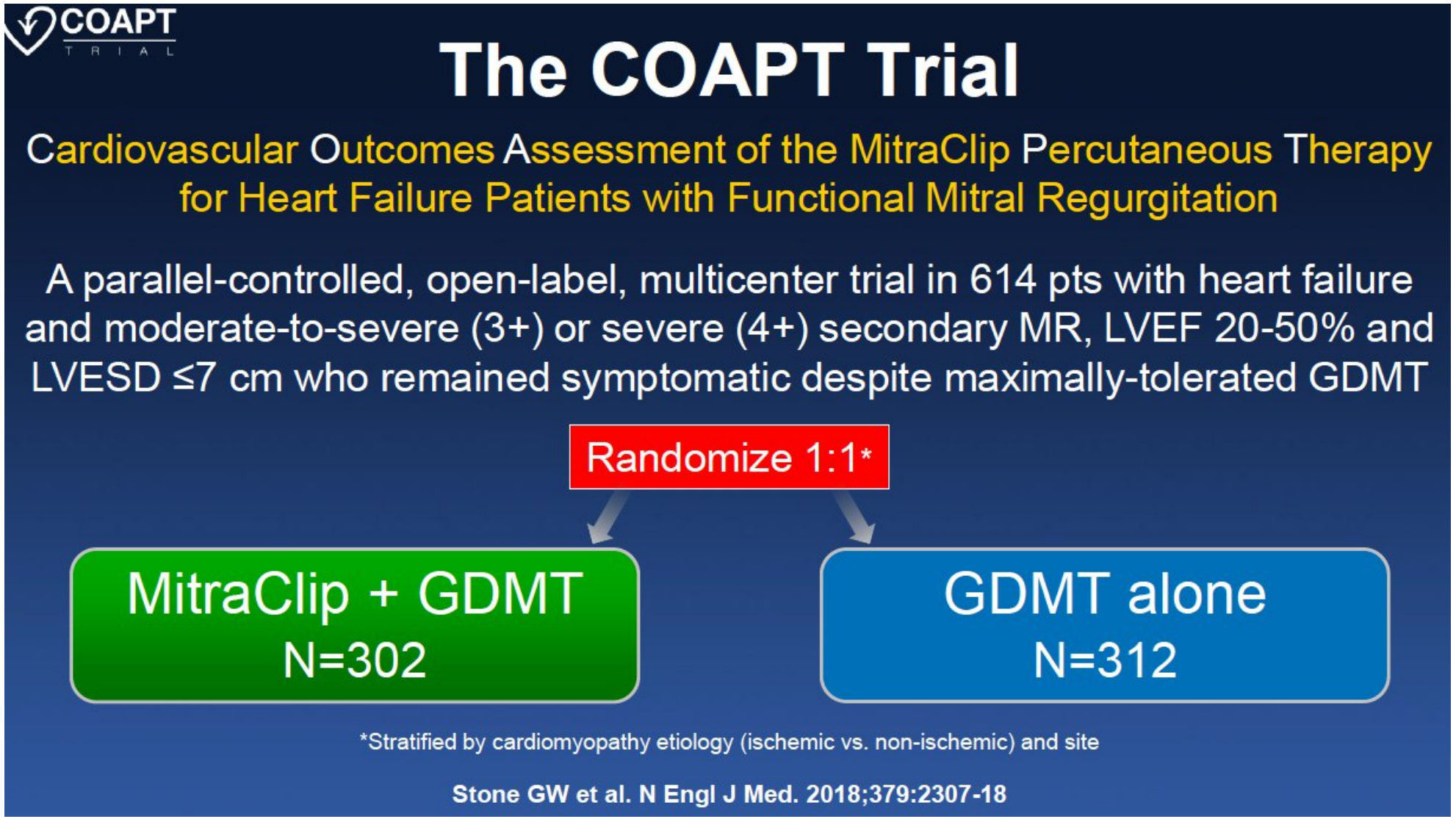
ESC Congress
Munich 2018

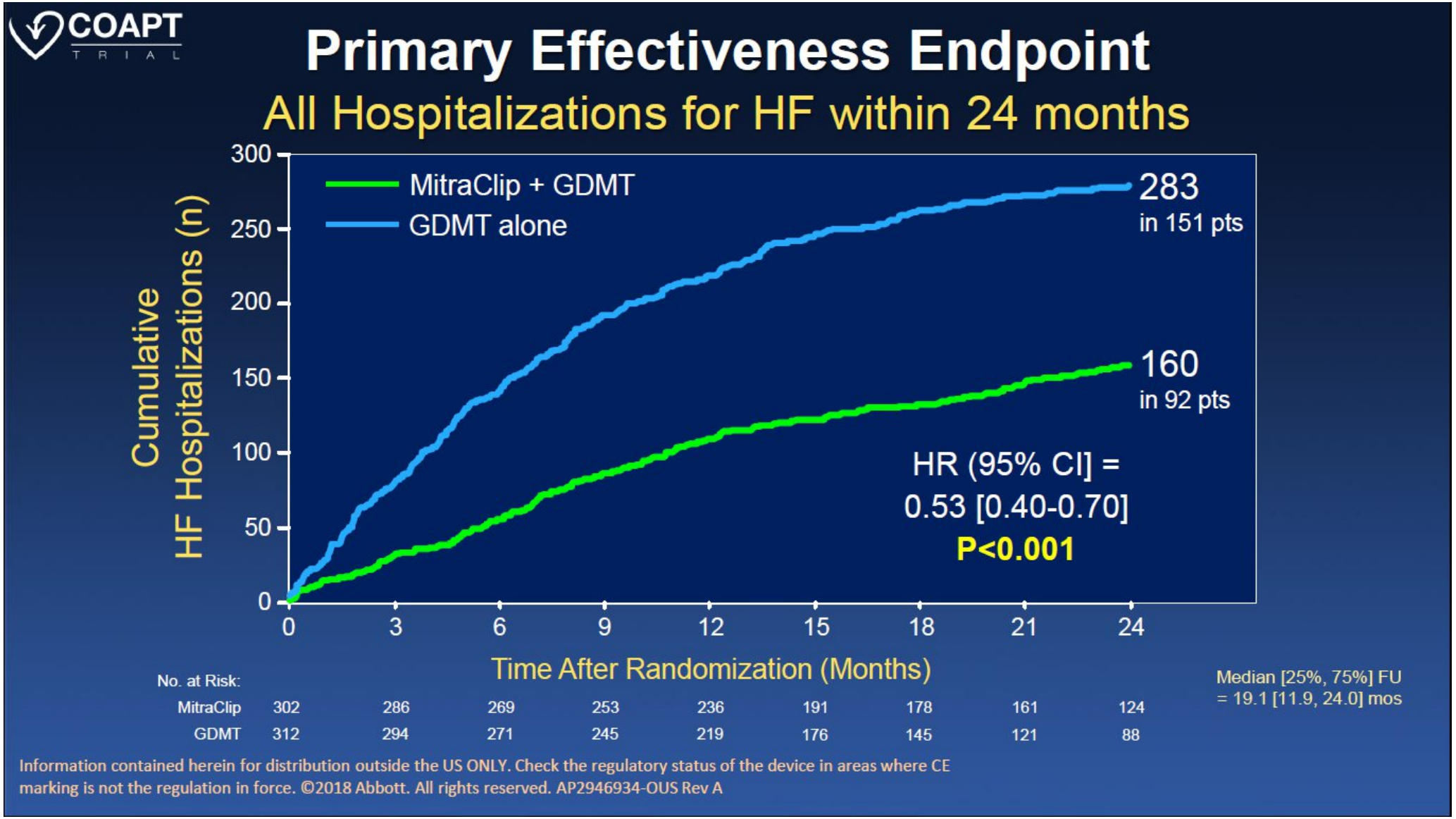
MITRA-FR



Final key message..
»Treat the muscle…
not the valve!»

COAPT – Trial Design




COAPT TRIAL
Primary Effectiveness Endpoint
All Hospitalizations for HF within 24 months
Cumulative HF Hospitalizations (n)
300
250
200
150
100
50
0
MitraClip + GDMT
GDMT alone
283
in 151 pts
160
in 92 pts
HR (95% CI] =
0.53 [0.40-0.70]
P<0.001
0
3
6
9
12
15
18
21
24
Time After Randomization (Months)
No. at Risk:
MitraClip 302 286 269 253 236 191 178 161 124
GDMT 312 294 271 245 219 176 145 121 88
Median [25%, 75%] FU
= 19.1 [11.9, 24.0] mos
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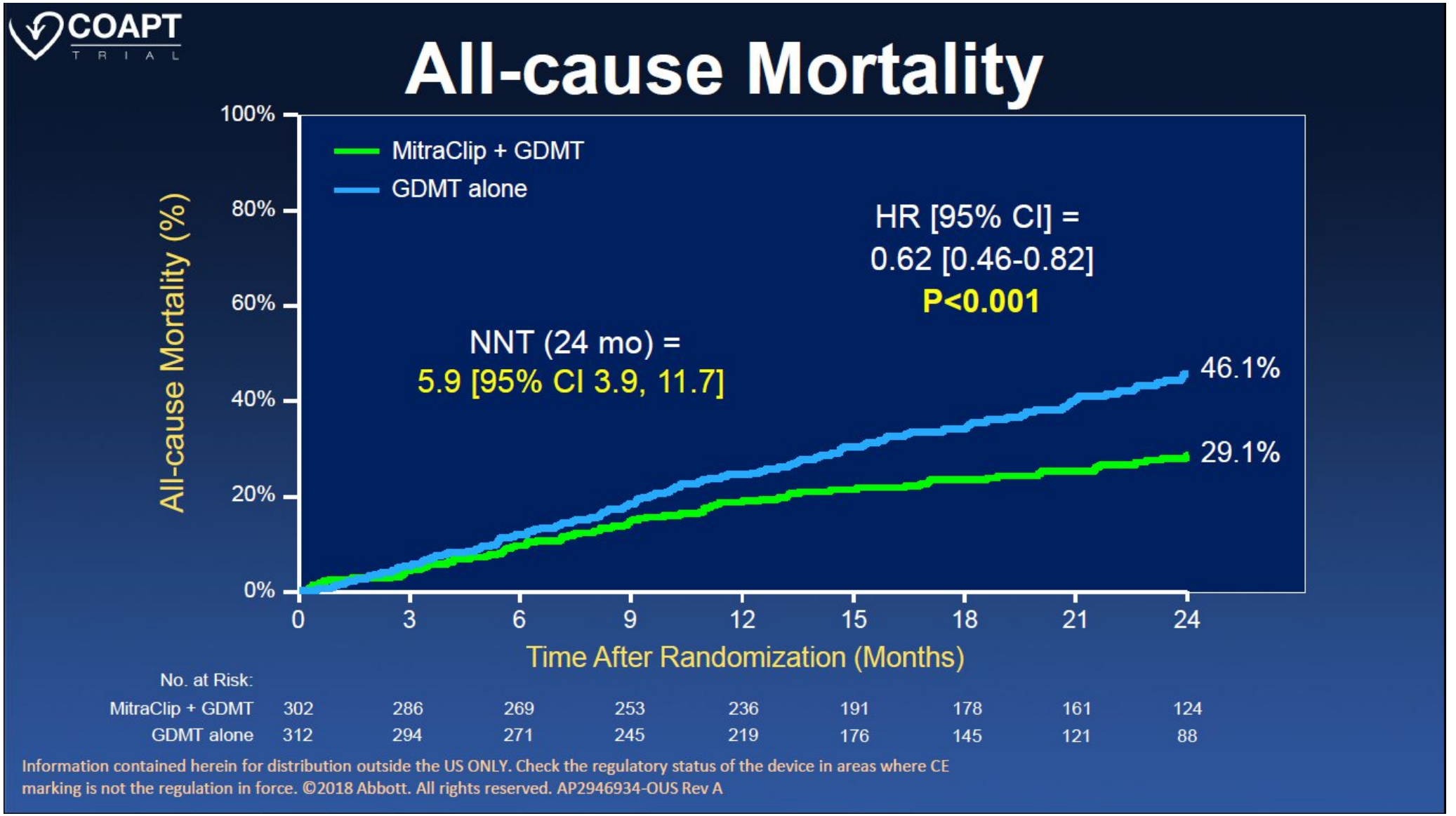
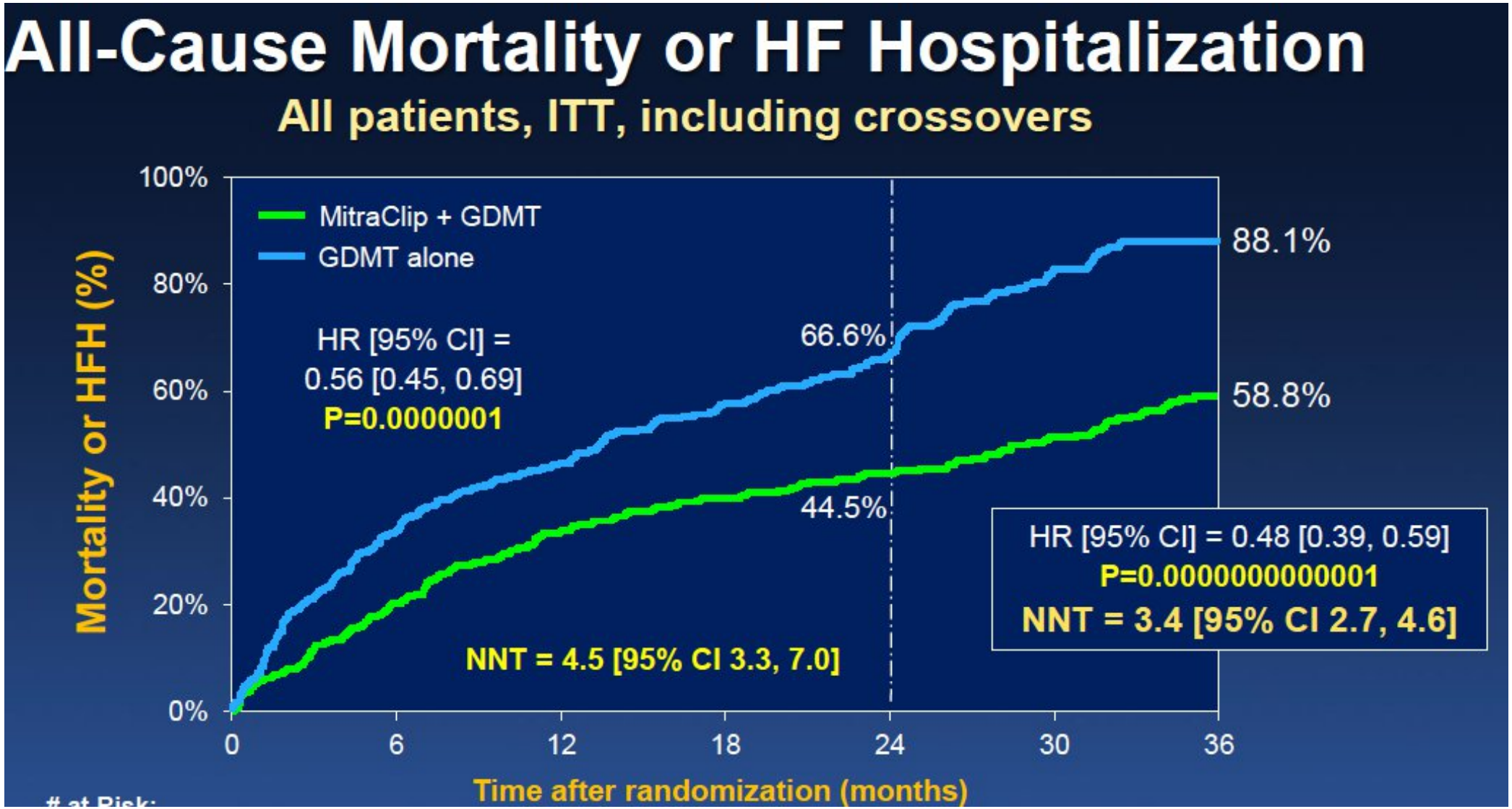

COAPT
TRIAL
All-cause Mortality
MitraClip + GDMT
GDMT alone
HR [95% CI] =
0.62 [0.46-0.82]
P<0.001
NNT (24 mo) =
5.9 [95% CI 3.9, 11.7]
46.1%
29.1%
All-cause Mortality (%)
100%
80%
60%
40%
20%
0%
0
3
6
9
12
15
18
21
24
Time After Randomization (Months)
No. at Risk:
MitraClip + GDMT 302 286 269 253 236 191 178 161 124
GDMT alone 312 294 271 245 219 176 145 121 88
Information contained herein for distribution outside the US ONLY. Check the regulatory status of the device in areas where CE marking is not the regulation in force. ©2018 Abbott. All rights reserved. AP2946934-OUS Rev A

COAPT – 36 Months



Differences between COAPT and MITRA-FR

	MITRA-FR (n=304)	COAPT (n=614)
Severe MR entry criteria	Severe FMR by EU guidelines: EROA >20 mm² or RV >30 mL/beat	Severe FMR by US guidelines: EROA >30 mm² or RV >45 mL/beat
EROA (mean ± SD)	31 ± 10 mm²	41 ± 15 mm²
LVEDV (mean ± SD)	135 ± 35 mL/m²	101 ± 34 mL/m²
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%

WHAT HAVE WE LEARNED?

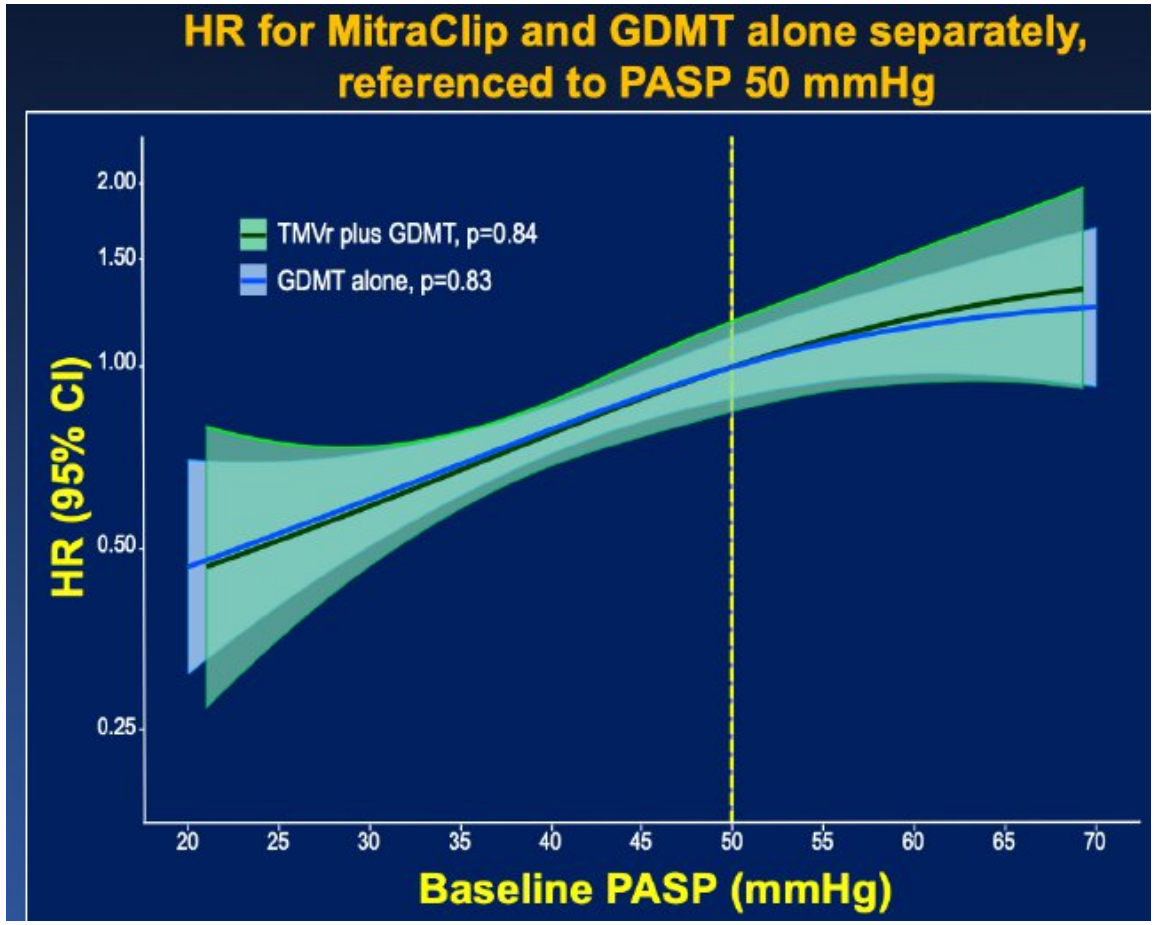
1) Come si spiegano i risultati contrastanti dei due trials?

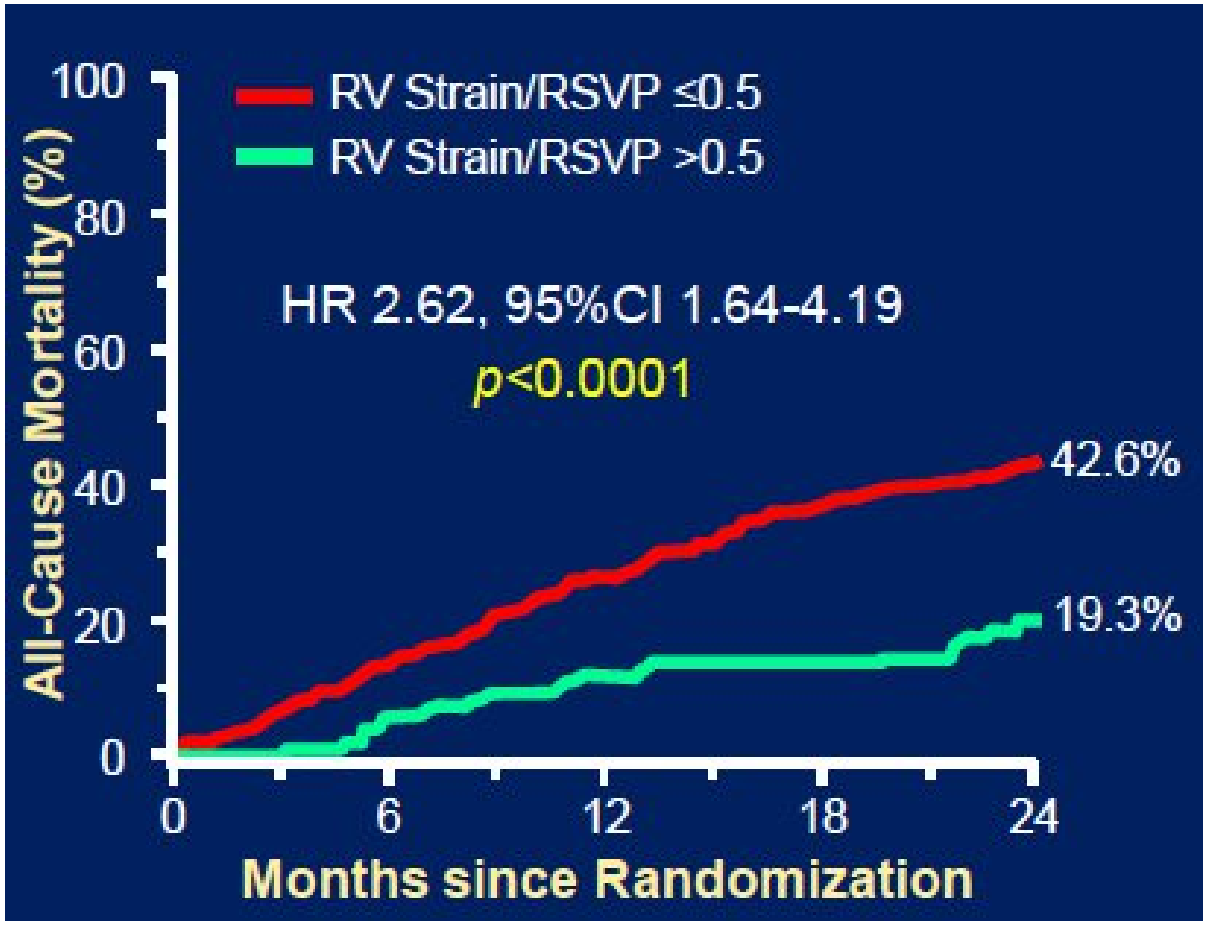
I pz MITRA-FR sono più “end stage” rispetto ai pz COAPT

2) Come possiamo far si che i pazienti beneficino al massimo dalla Mitraclip?

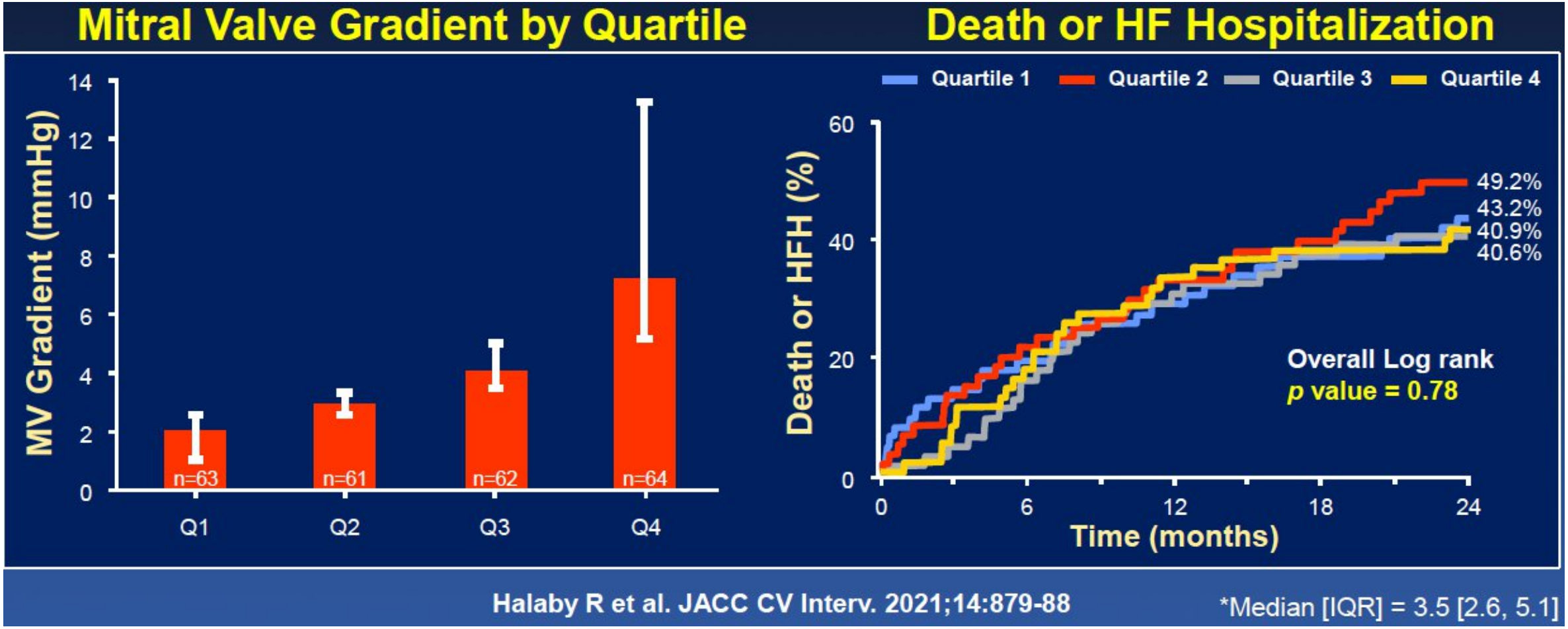
Timing precoce della procedura

Impact of Pulmonary HTN or RV-PA Coupling





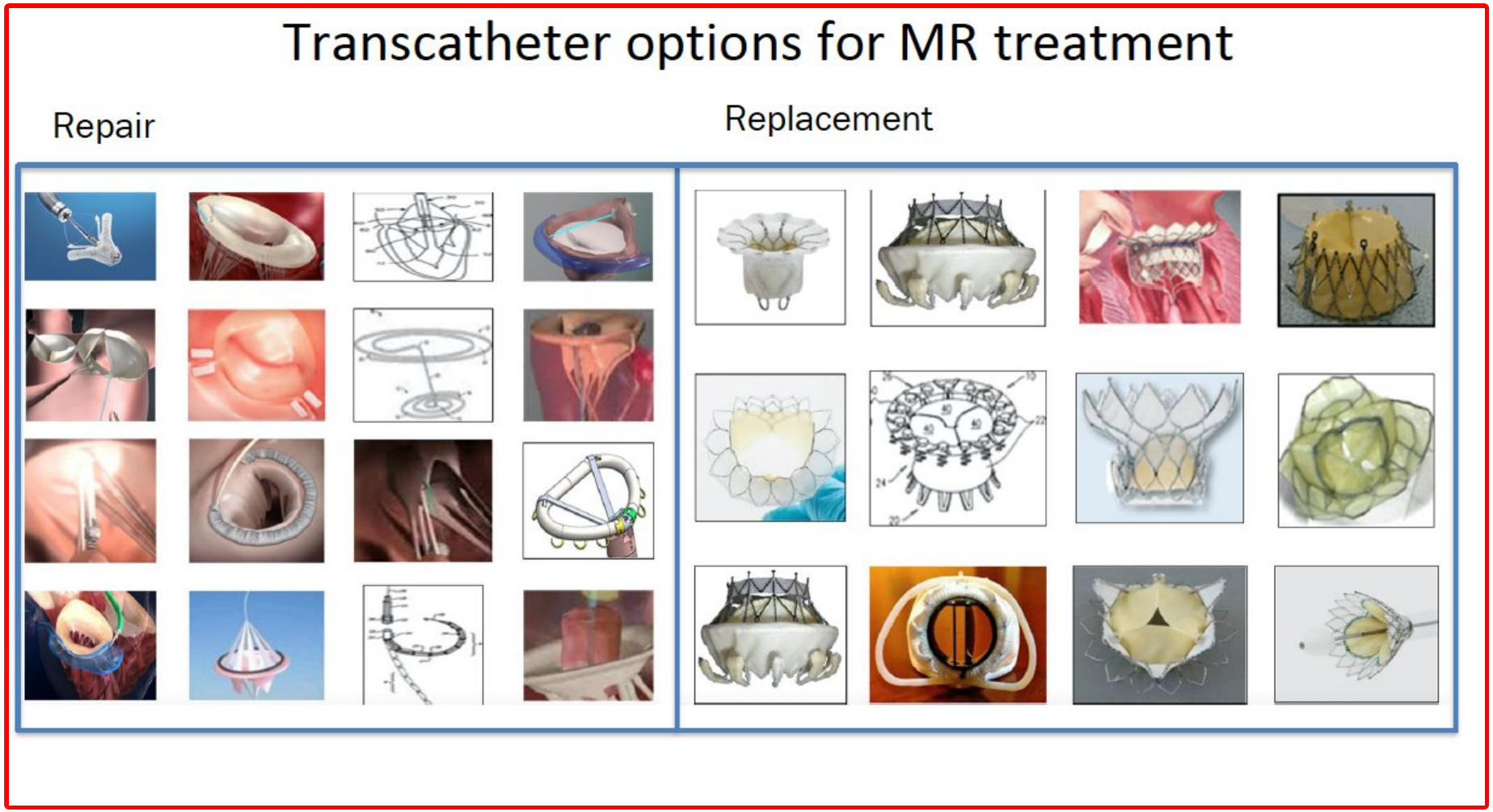
Impact of Post-Clip MV Gradient



WHAT WILL WE EXPECT?

- ✓In 2019 MitraClip rec eived FDA approval for FMR
- ✓With COAPT and recent advances in the treatment of FMR, a new paradigm has emerged –TEER has become ascendent
- ✓However, due to significant variability in Mitral Valve anatomy, not all patients are suitable for TEER
- ✓As a result, there is a clear unmet clinical need represented by patients with FMR not suitable for TEER

Transcatheter Approach to FMR



Tendyne Mitral Valve (CE Mark 2020)