MitraClip in Functional MR Patients : Japanese Initial Experience

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Mitral Regurgitation (MR)

Degenerative (Primary) MR: Disorder of the Mitral Valve Apparatus (leaflets, chords, papillary muscle)

Valve makes the Ventricle Sick

Mechanical Solution: Open Surgical

Functional (Secondary) MR: Leaflets appear normal, MR due to abnormal LV/LA geometry

Ventricle makes the Valve Sick

Medical treatment for LV dysfunction
Surgical reduction of MR ?

ESC Guideline 2017

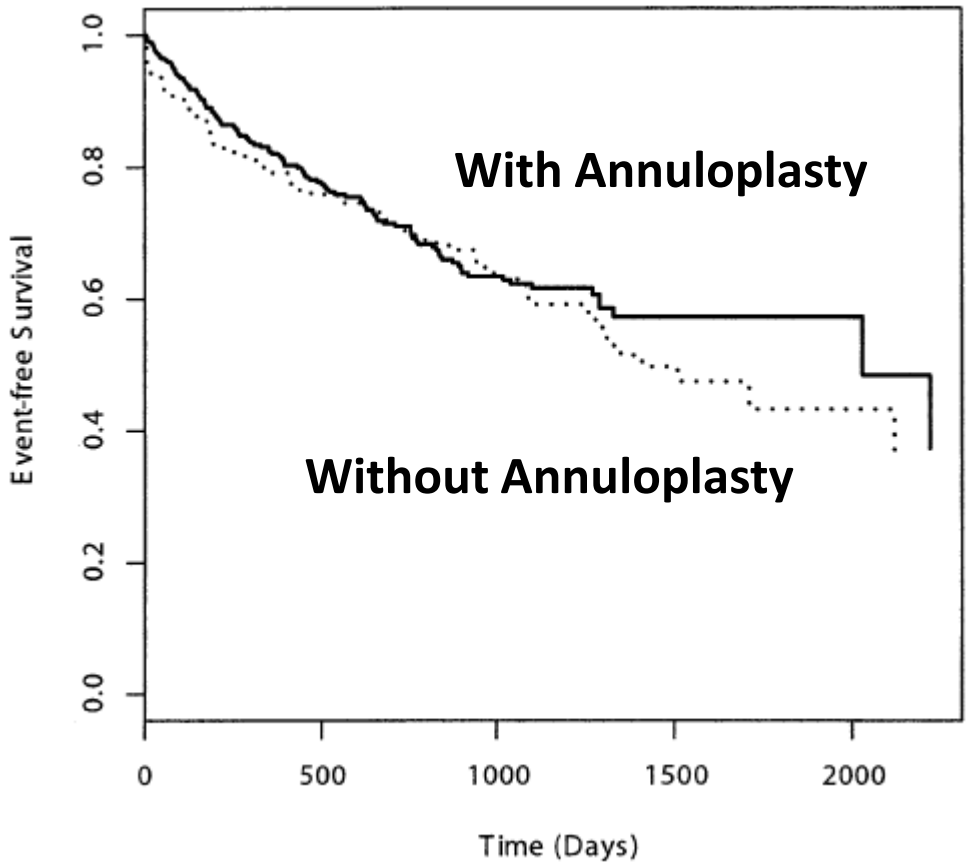
For isolated secondary (functional) MR…

- Surgery = Class IIb in LVEF >30%
- MitraClip = Class IIb regardless of LVEF

When revascularization is not indicated, surgery may be considered in patients with severe secondary mitral regurgitation and LVEF >30% who remain symptomatic despite optimal medical management (including CRT if indicated) and have a low surgical risk.	IIb	C
When revascularization is not indicated and surgical risk is not low, a percutaneous edge-to-edge procedure may be considered in patients with severe secondary mitral regurgitation and LVEF >30% who remain symptomatic despite optimal medical management (including CRT if indicated) and who have a suitable valve morphology by echocardiography, avoiding futility.	IIb	C
In patients with severe secondary mitral regurgitation and LVEF <30% who remain symptomatic despite optimal medical management (including CRT if indicated) and who have no option for revascularization, the Heart Team may consider a percutaneous edge-to-edge procedure or valve surgery after careful evaluation for a ventricular assist device or heart transplant according to individual patient characteristics.	IIb	C

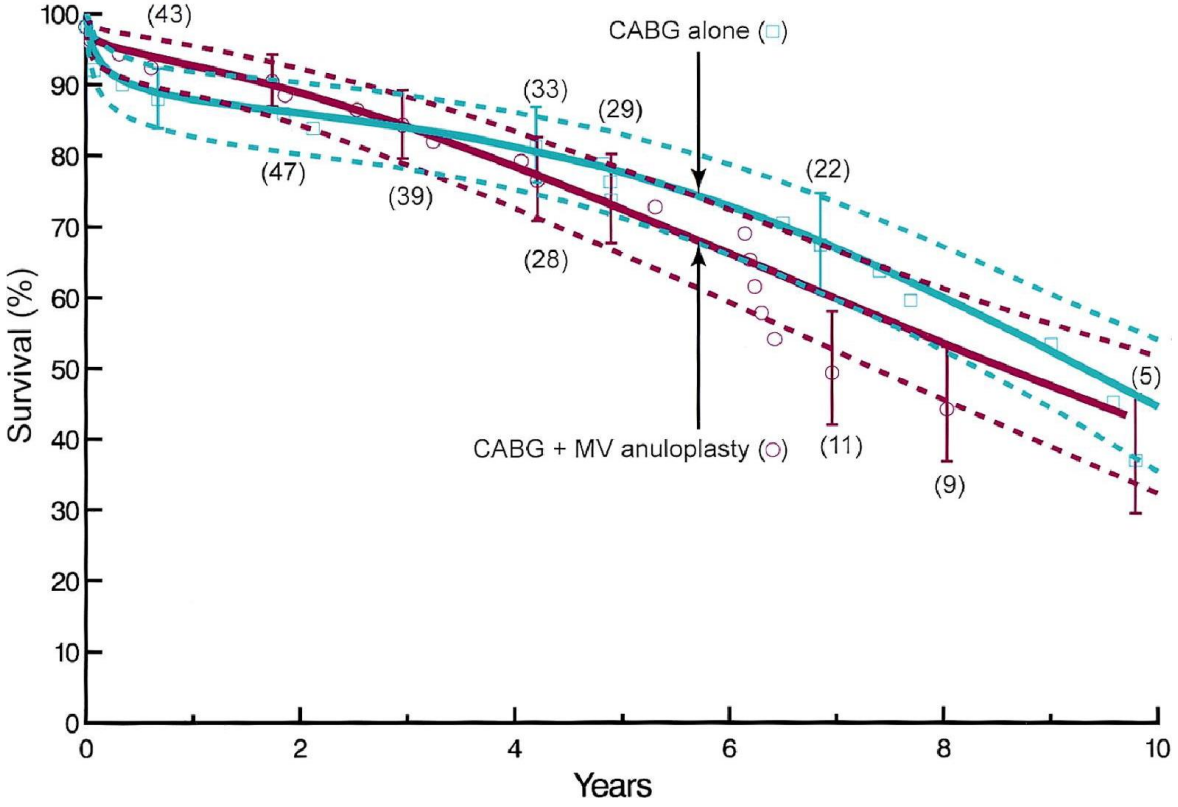
Surgery for Functional MR

FMR with LV dysfunction



J Am Coll Cardiol. 2005;45(3):381-7.

Ischemic MR



J Am Coll Cardiol. 2007;49(5):2191-2201.

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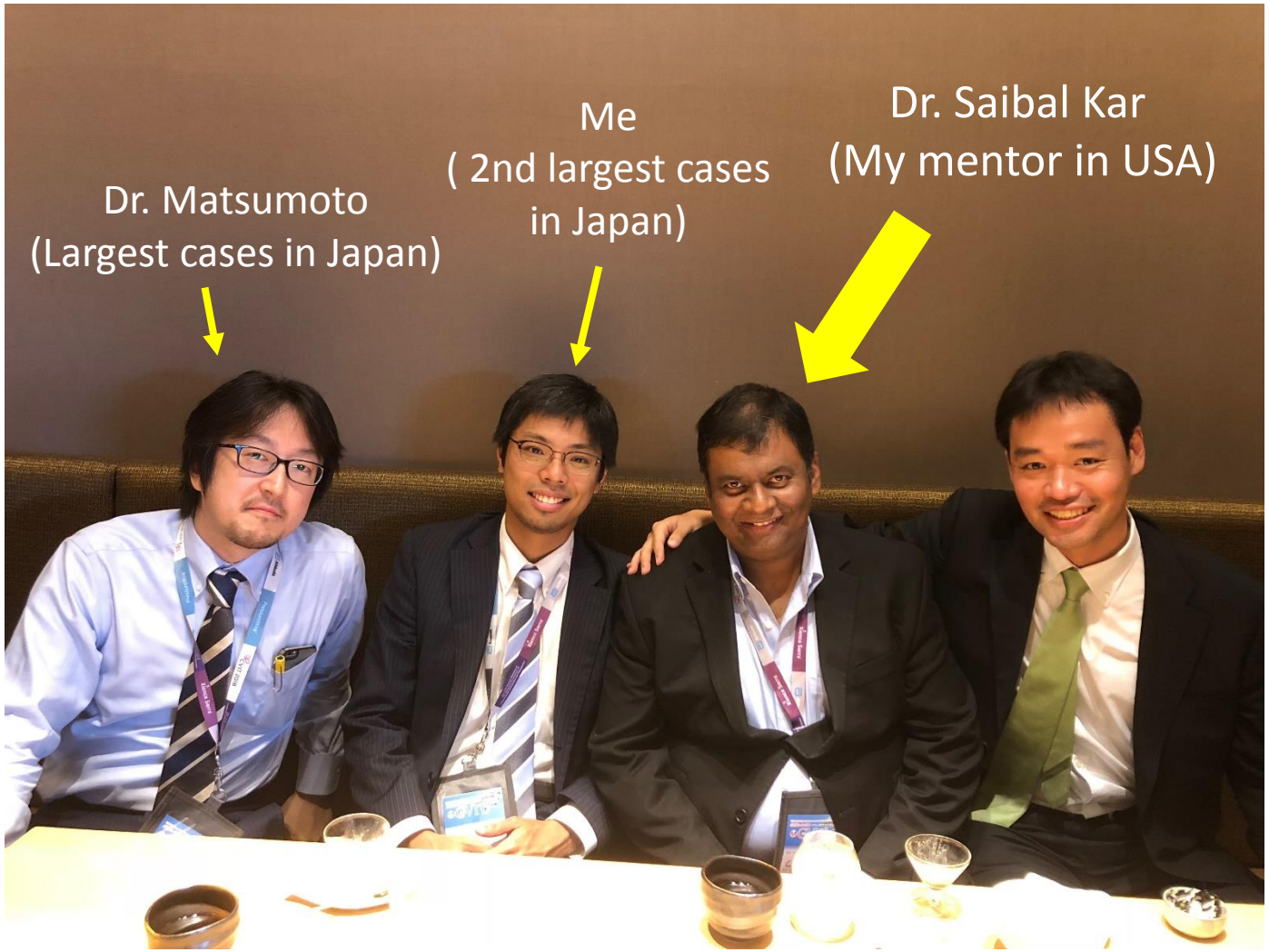
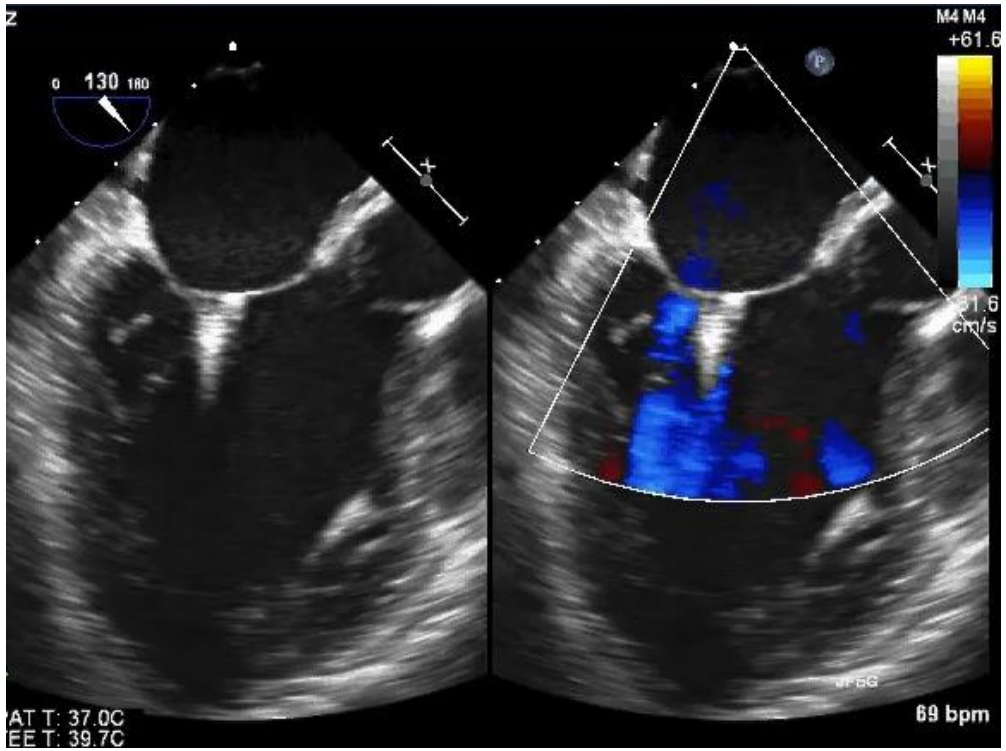
MitraClip for Functional MR





CVIT 2018 in Kobe, Japan

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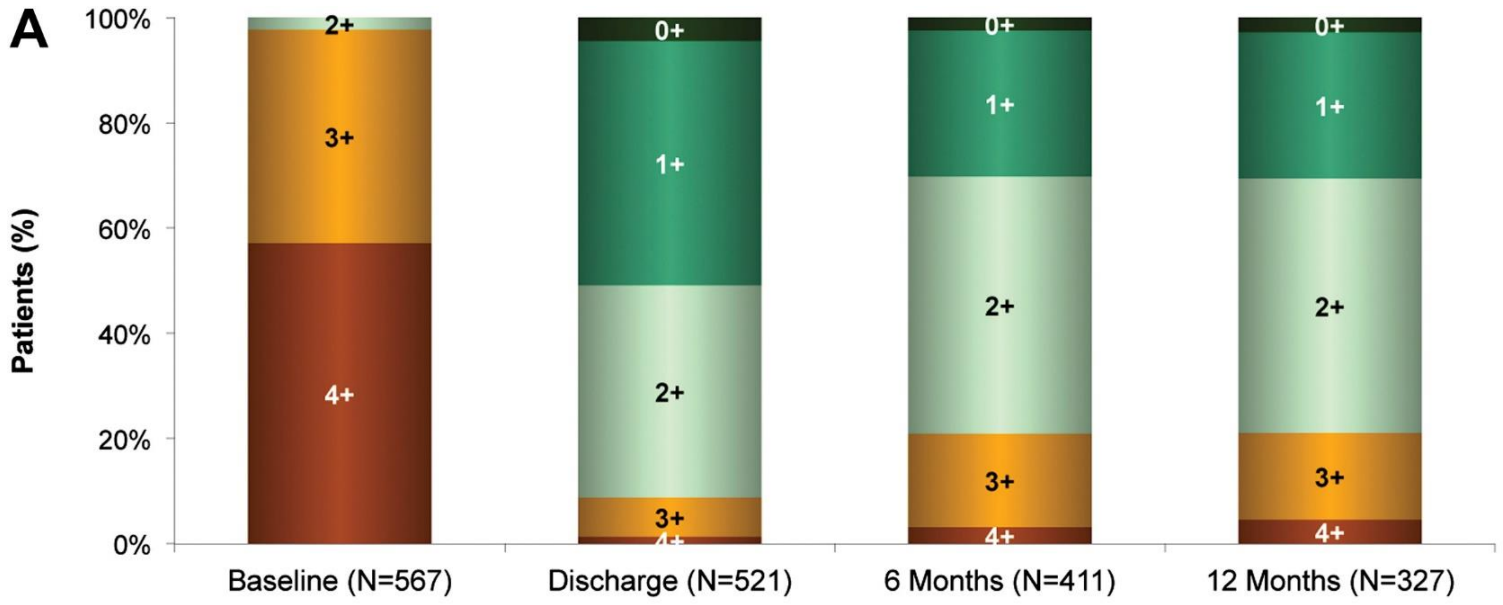
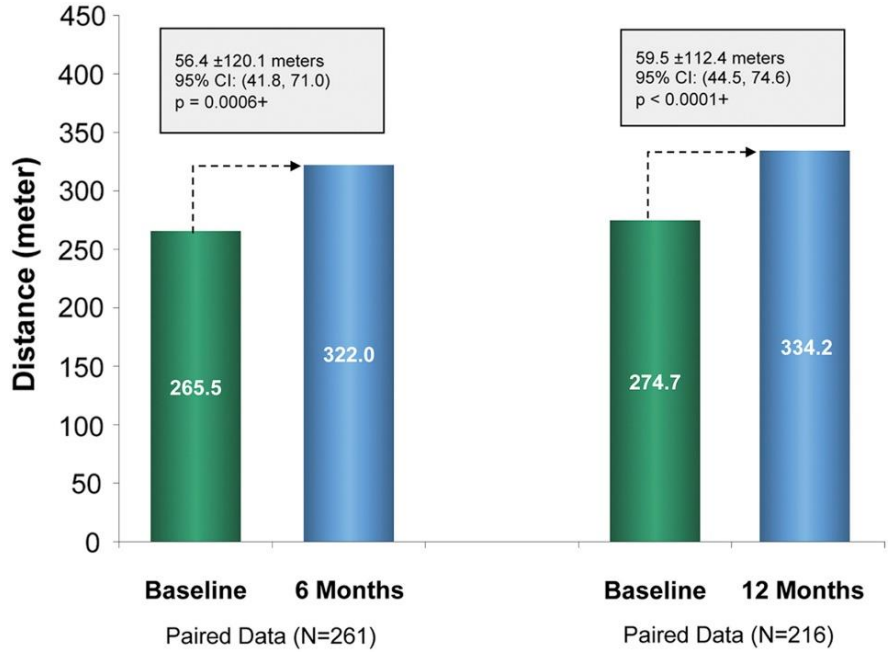
European Real-World ACCESS-EU Registry

FMR: 77% of Study Population

MR Grade



6-minites Walk



Mean age = 73.7 years, LVEF<40% = 52%, NYHA 3/4= 84.9%

1-month mortality = 3.4%, 1-year mortality = 17.1%

J Am Coll Cardiol. 2013;62(12):1052-1061.

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Clinical Implication of Functional MR Reduction

Compared with optimal medical therapy…

Does MitraClip

- improve clinical symptoms？
- improve cardiac function？
- reduce heart failure hospitalization？
- improve mortality？

COAPT TRIAL

COAPT

A Randomized Trial of Transcatheter Mitral Valve Leaflet Approximation in Patients with Heart Failure and Secondary Mitral Regurgitation

Gregg W. Stone, MD

On behalf of Michael Mack, William Abraham, JoAnn Lindenfeld and the COAPT Investigators

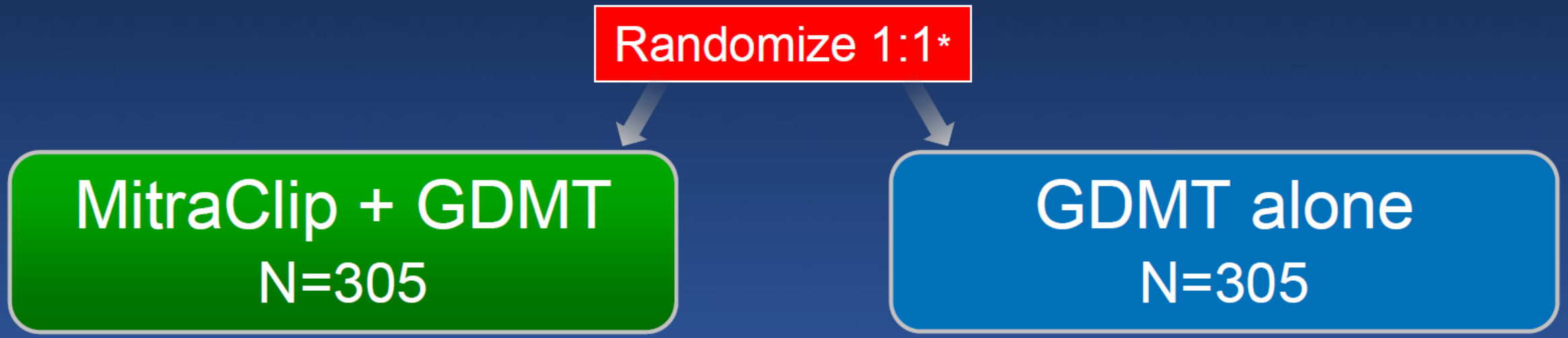
Stone GW, et al. N Engl J Med. 2018 ahead of print.

COAPT TRIAL

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



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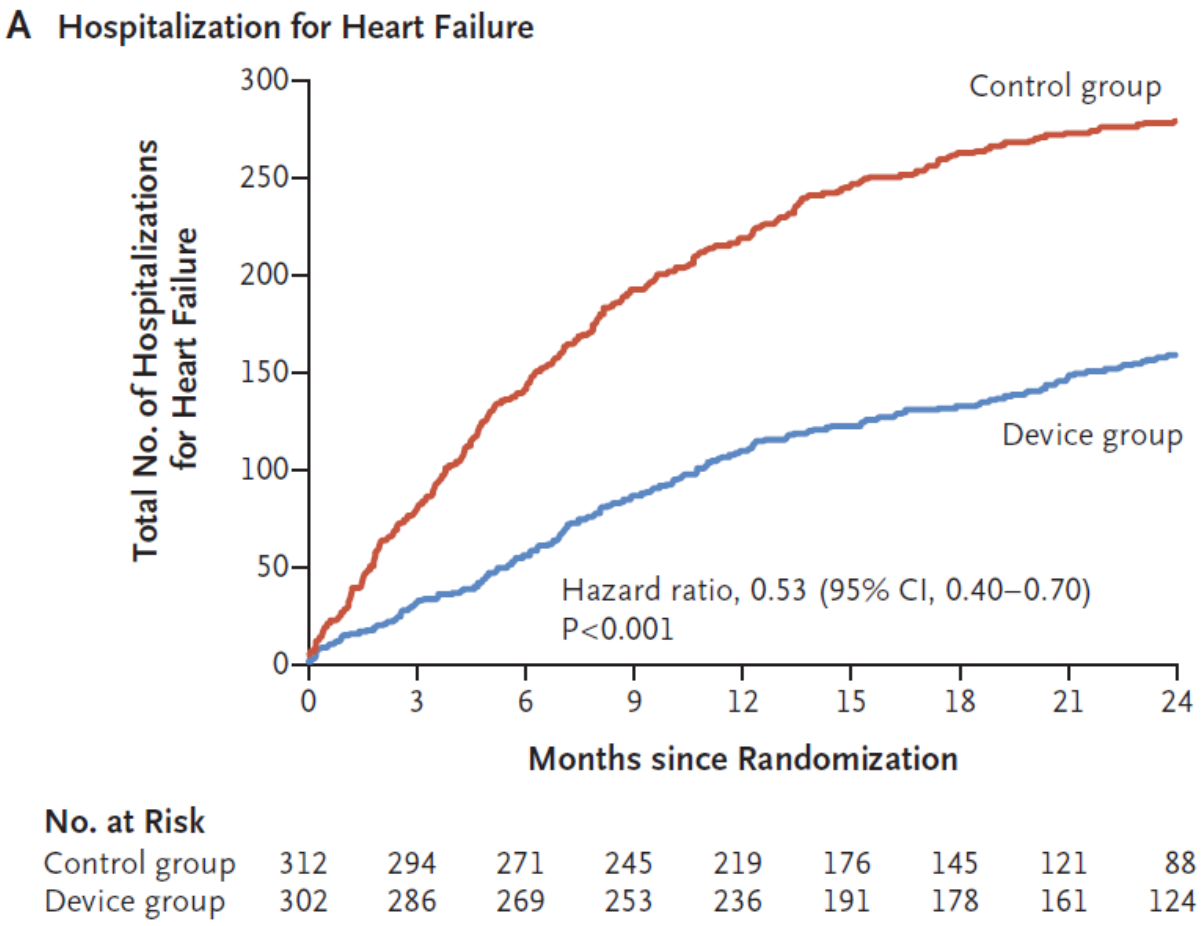
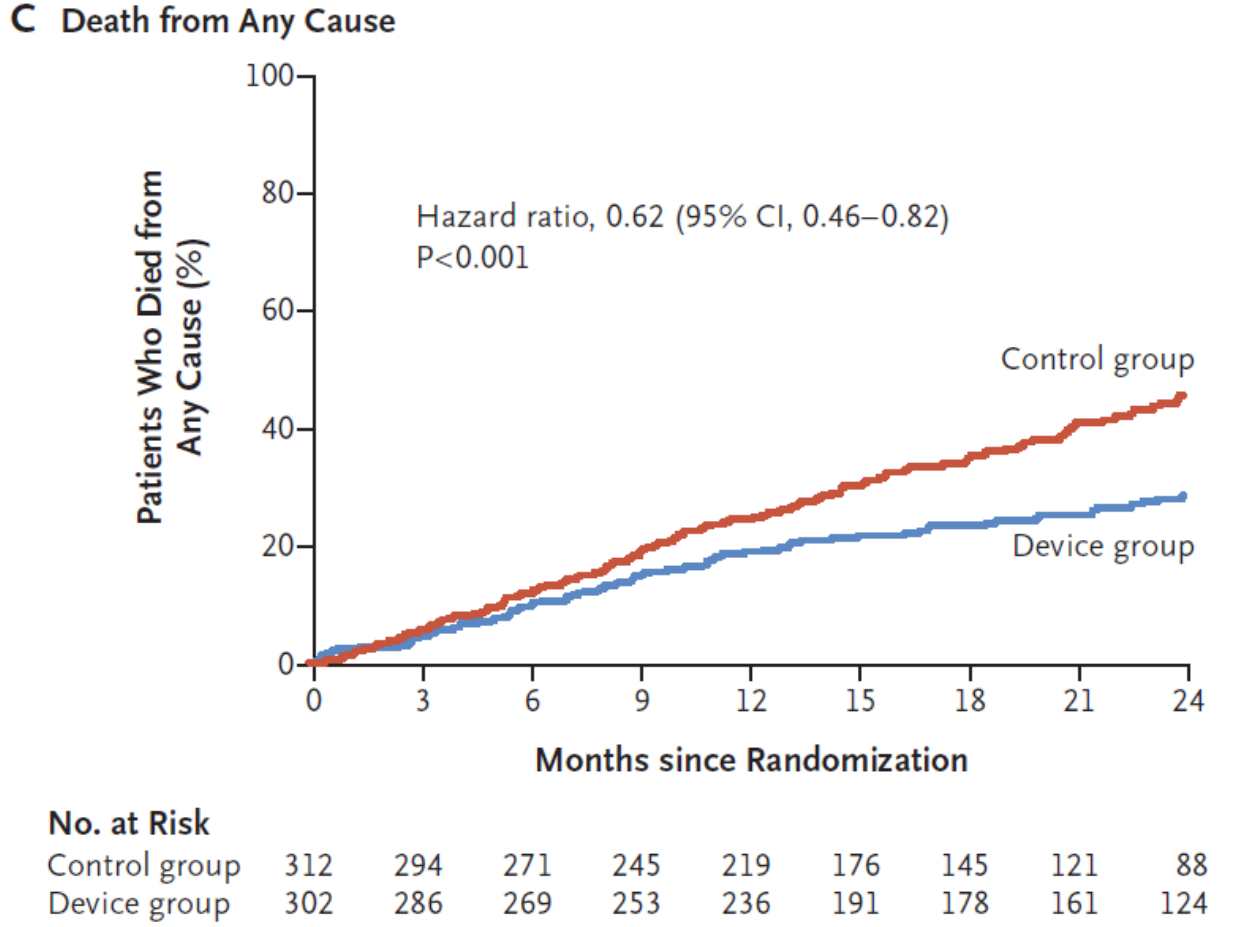
COAPT Trial





MitraClip reduce not only HF hospitalization but also all-cause and cardiac mortality.
The first therapy to show the clinical benefit for FMR reduction in HF patients.

Stone GW, et al. N Engl J Med. 2018 ahead of print.

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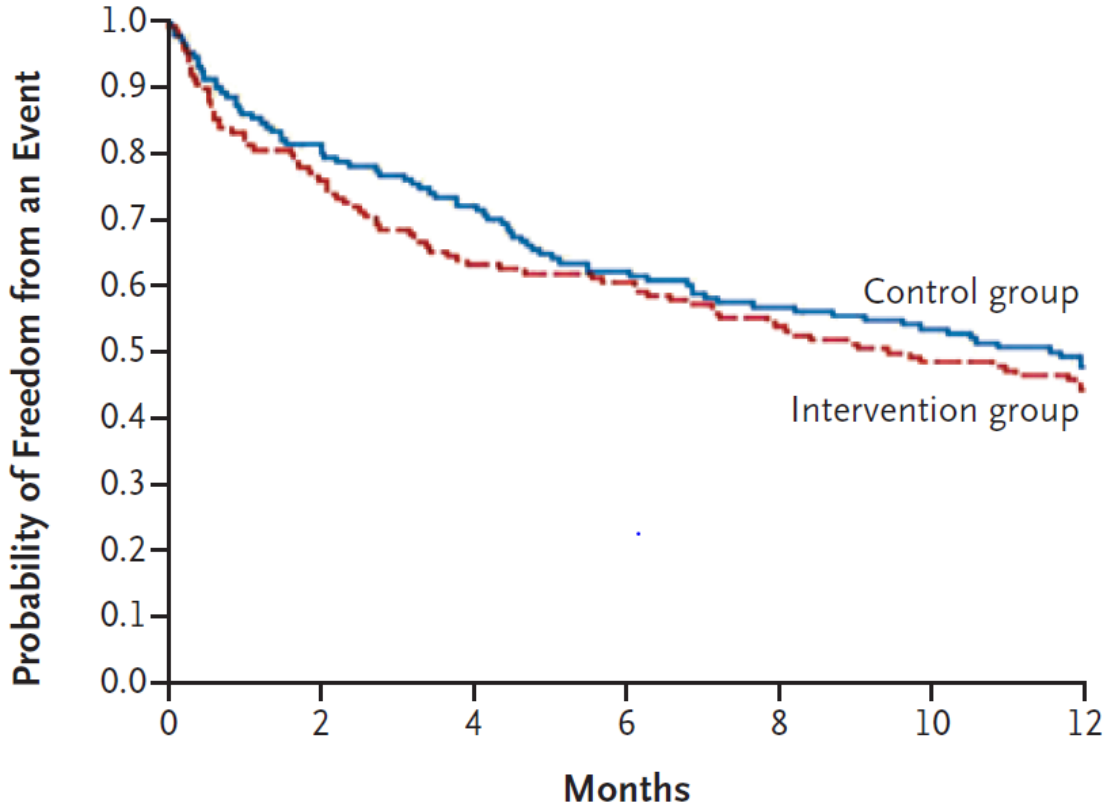
Mitra-FR Trial

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*

Non significant difference in mortality and HF hospitalization between OMT and MitraClip



No. at Risk							
Control group	152	123	109	94	86	80	73
Intervention group	151	114	95	91	81	73	67

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Potential Reasons of Difference

	Mitra-FR (n=304)	COAPT (n=614)
Severe MR Definition	ESC guidelines EROA>0.2cm^2 or RV>30ml Mean EROA = 0.31±10 cm^2	US guidelines EROA>0.3cm^2 or RV>45ml Mean EROA = 0.41±15 cm^2
LVEDV (ml)	135±35 ml/m^2	101±34 ml/m^2
Guideline directed medial therapy	Real-world practice ⇒Change of regimen from baseline to Follow-up	CEC confirmed maximum DMT before enroll ⇒No change from baseline to follow-up
Acute results：No clip/≥3+ MR	9% / 9%	5% / 5%
Procedural complications	14.6%	8.5%
12 month f/u MR ≥3+	17%	5%

Indication of MitraClip in Japan

MitraClip was approved for high surgical risk patients with symptomatic severe MR (grade 3+ or 4+ at rest or exercise) with **LV ejection fraction more than 30%**.

Exclusion criteria…

- Functional MR patients under suboptimal GDMT
- Acute worsened MR
- Catecholamine dependent (supported is OK ?)
- Under support device such as ECMO, IABP, and Impella

Japanese Experience

April 2018 to October 2018

Total Number : 261 patients

Degenerative MR: 71 patients

Functional MR: 194 patients (74.3%)

Acute procedural success: 91.1%

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April 2018 to December 2018

We treated 36 patients with severe MR using MitraClip

Degenerative MR: 5 patients

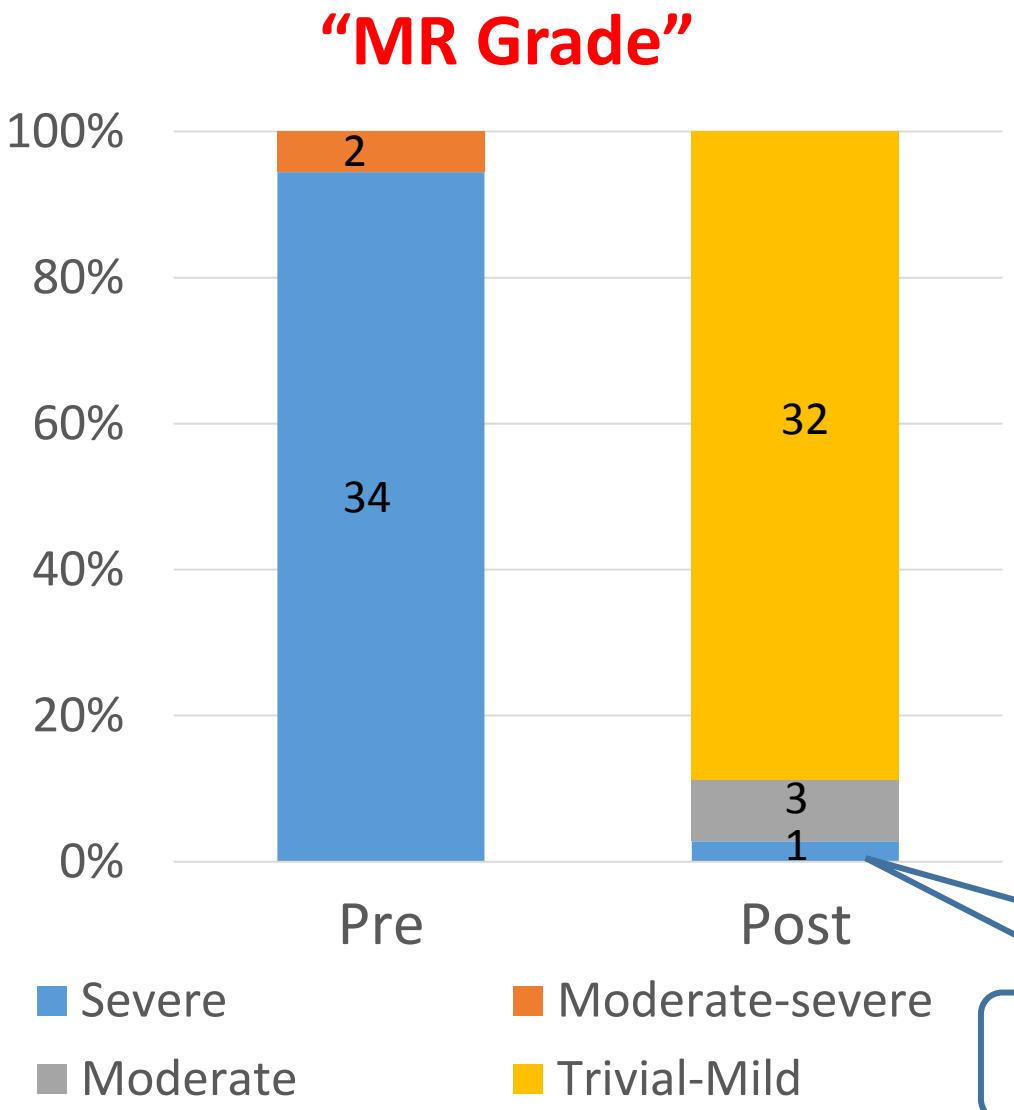
Functional MR: 31 patients

Patient Backgrounds

N = 36

Age	73.0 ± 11.4	DMR/FMR	5 (13.9)/31 (86.1)
Male	18 (50.0)	FMR	
Hypertention	13 (36.1)	Nonischemic-MR	15 (41.7)
Diabetes	12 (33.3)	Ischemic-MR	11 (30.6)
Prior MI	10 (27.8)	Atrial-MR	5 (13.9)
HF admission (<1 year)	24 (66.7)	Severe MR	34 (94.4)
AF	26 (72.2)	EROA, cm2	0.57 ± 0.50
STS score	11.3 ± 8.1	LVDd, mm	56.8 ± 9.3
BNP, pg/dl	559 ± 492	LVDs, mm	45.0 ± 14.4
BSA, m2	1.49 ± 0.16	LVEF, %	42.4 ± 15.1
eGFR	39.7 ± 22.3	LA diameter, mm	51.1 ± 10.7
NYHA class 3/4	16 (44.4)/12 (33.3)	PASP, mmHg	37.9 ± 17.1
CRT implantation	7 (28.0)		
Catecholamine div	4 (11.1)		

Procedural Results



N = 36	
Procedural success	35 (97.2)
Days to discharge	7.1 ± 5.5 days
Number of clips	1.42 ± 0.55
Fluoroscopic time	19.7 ±12.9 min
Procedure time	107 ± 56 min
Post MV pressure gradient	2.6 ± 1.2 mmHg
Hematoma (transfusion)	1 (2.8)
Iatrogenic ASD closure	3 (8.3)
Pericardial effusion	1 (2.8)

Leaflet tear by leaflet grasping

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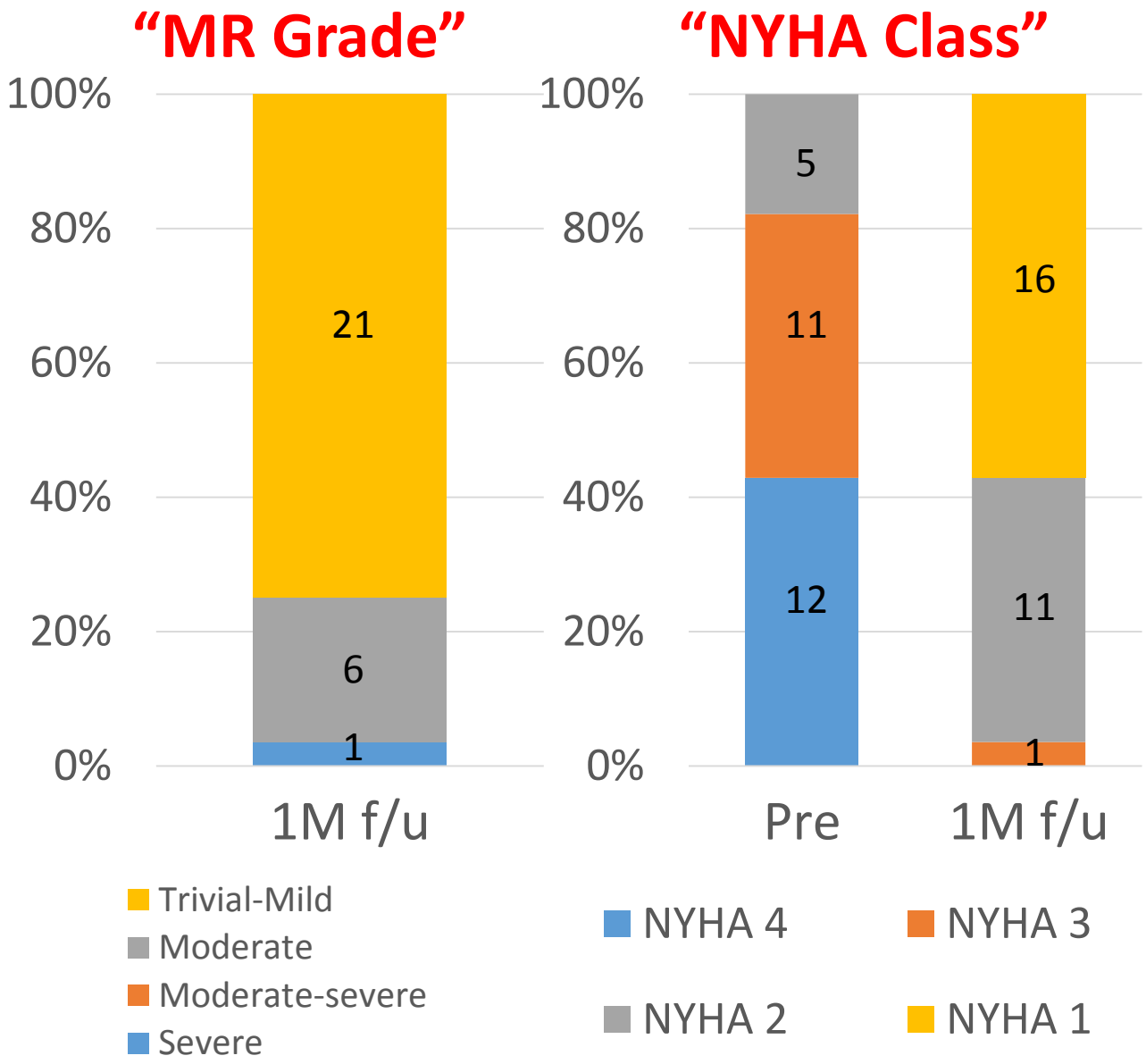
1-Month Follow-up (n = 28)



N = 28	
Death	0
Hospitalization for HF	0
Open heart surgery	0
LVEF	38.4 ± 22.9%
	(pre) 41.1±14.3%
MV mean pressure gradient	3.1 ± 1.4 mmHg
PASP	31.3 ± 9.2 mmHg
	(pre) 36.2±17.0 mmHg
BNP	522 ± 512 pg/dl
	(pre) 575±469 pg/dl
eGFR	35.1±15.7
	(pre) 35.9±14.5
5m walk	7.7±5.0 sec
	(pre) 8.8±6.5 sec

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Types of Functional MR

- Ischemic MR
- Non-ischemic MR
  - DCM (Sometimes difficult due to restrictive posterior leaflet)
  - HCM (Technically easy because of sufficient leaflet length)
  - Atrial MR (Most difficult type in functional MR)

Types of Functional MR

- **Ischemic MR**
- Non-ischemic MR
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Case Summary

Patient Demographics

- Age: 74 years
- Gender: Male

Risk Score

- STS score 10.4% for replacement
- Clinical frailty scale = 2

Past Medical History

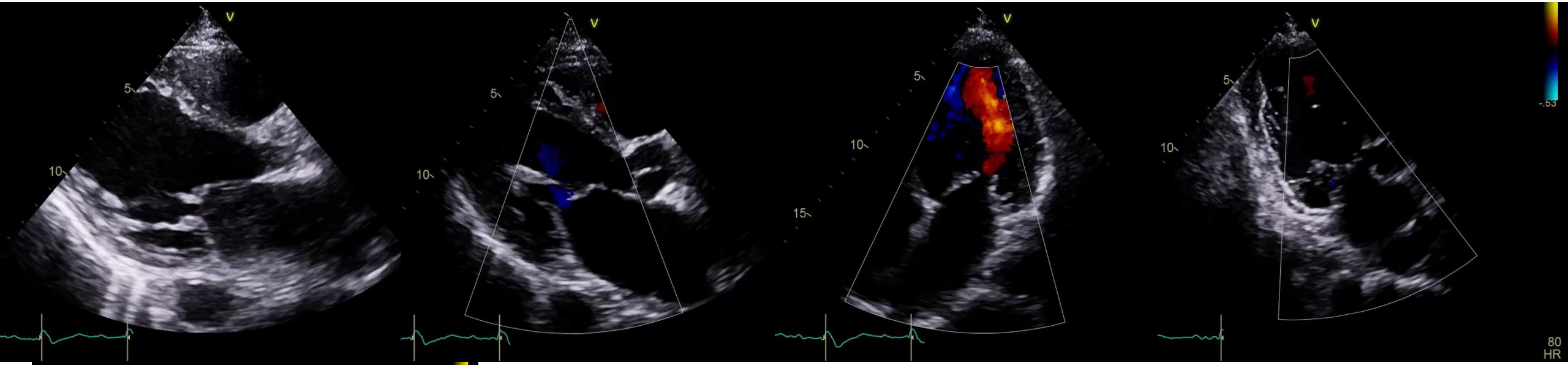
- CKD (eGFR = 25)
- AMI (PCI for LAD/LCX with IABP)
- 2 times HF hospitalization within 6 months

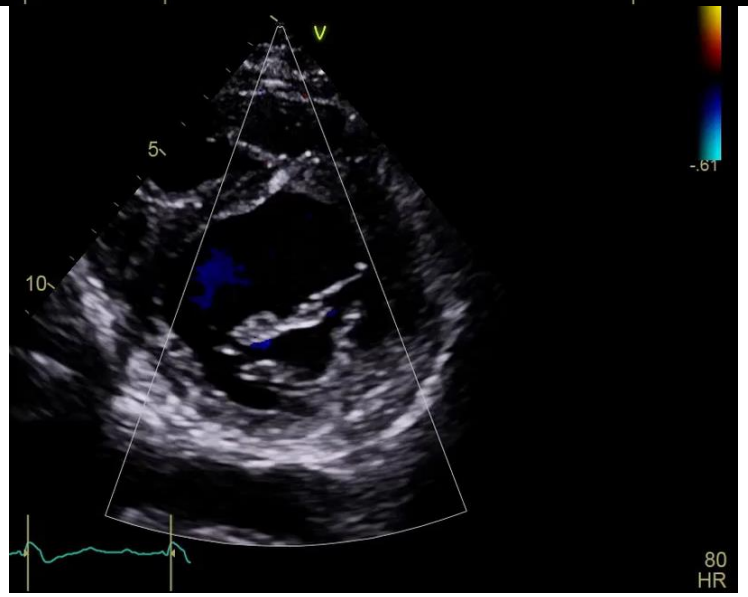
Clinical Presentation

- Dyspnea（NYHA class 4）
- Orthopnea
- Low output syndrome on dobutamine

Ischemic MR with severe LV dysfunction

Baseline TTE





MR grade	Severe	Forward SV	25 ml
EROA	0.84 cm^2	LVEF	31%
LVDd/Ds	62/48 mm	MVA	5.56 cm^2
TR grade	Mild	TR-PG	65 mmHg

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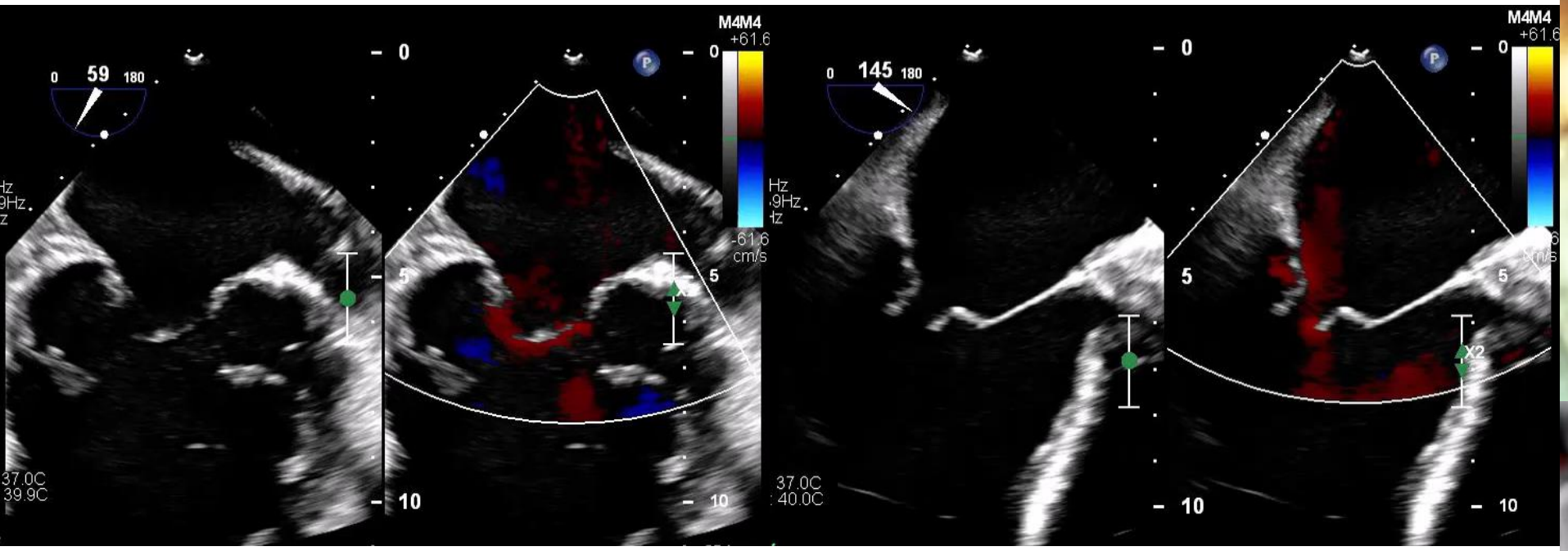
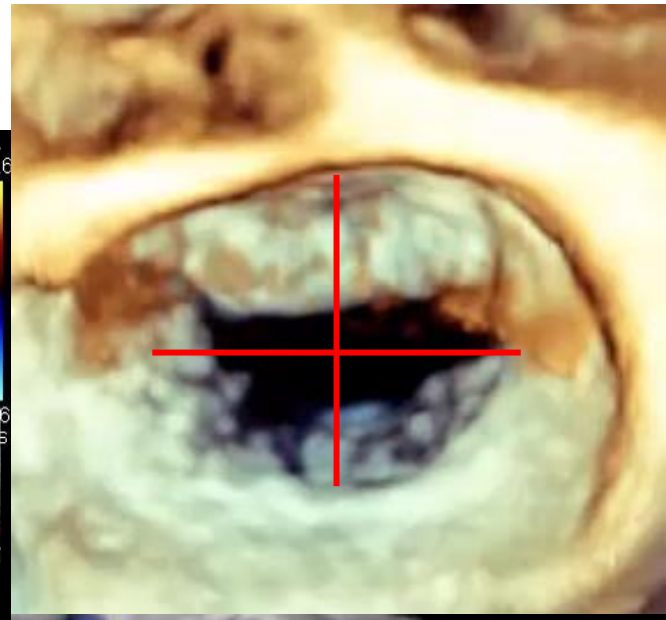
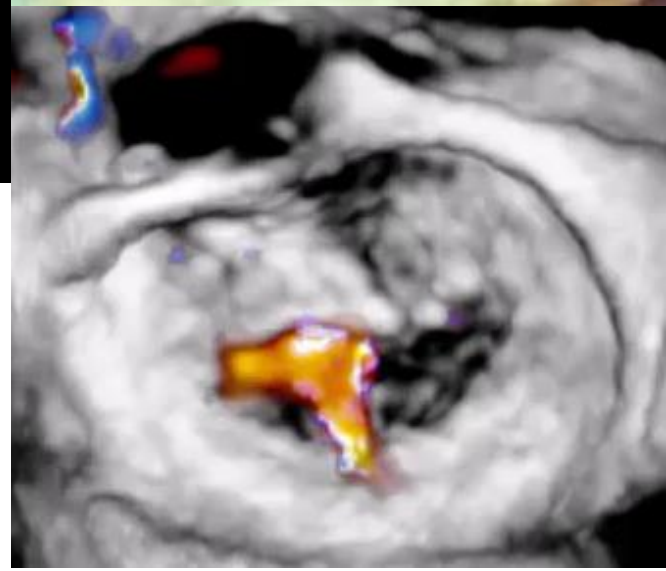
Baseline TEE







Wide central MR from A2/P2
Small gap in 3DTEE
Sufficient PML length for leaflet grasping

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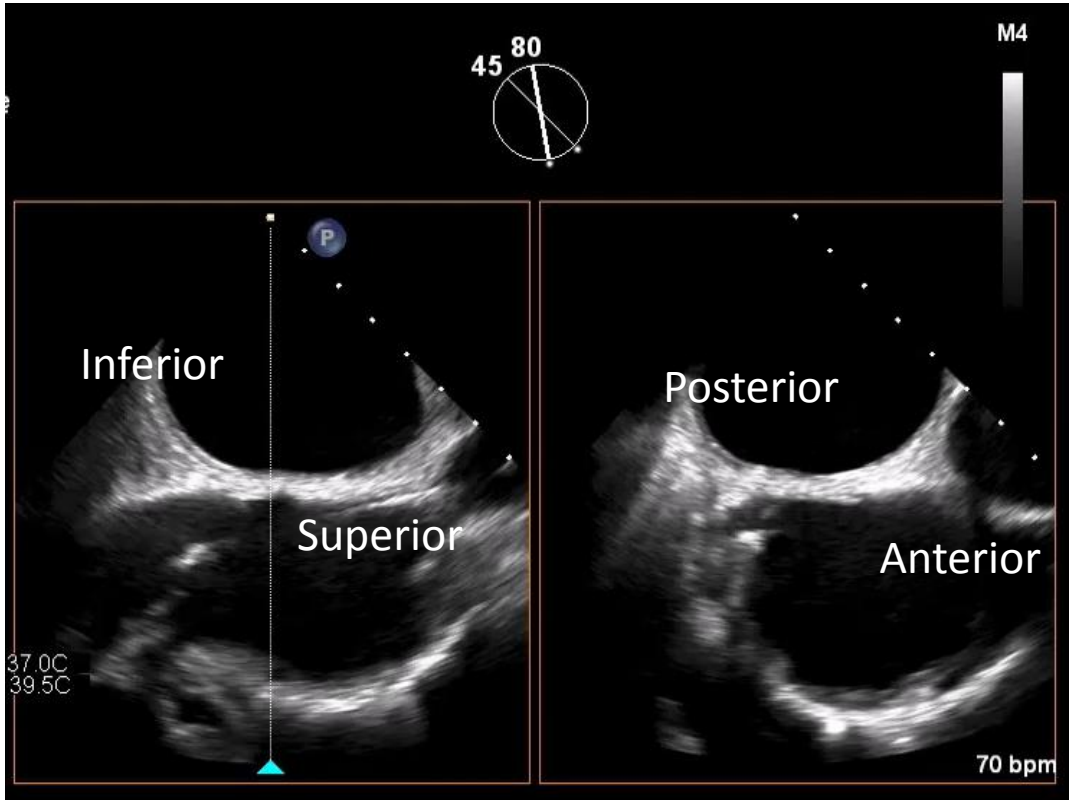
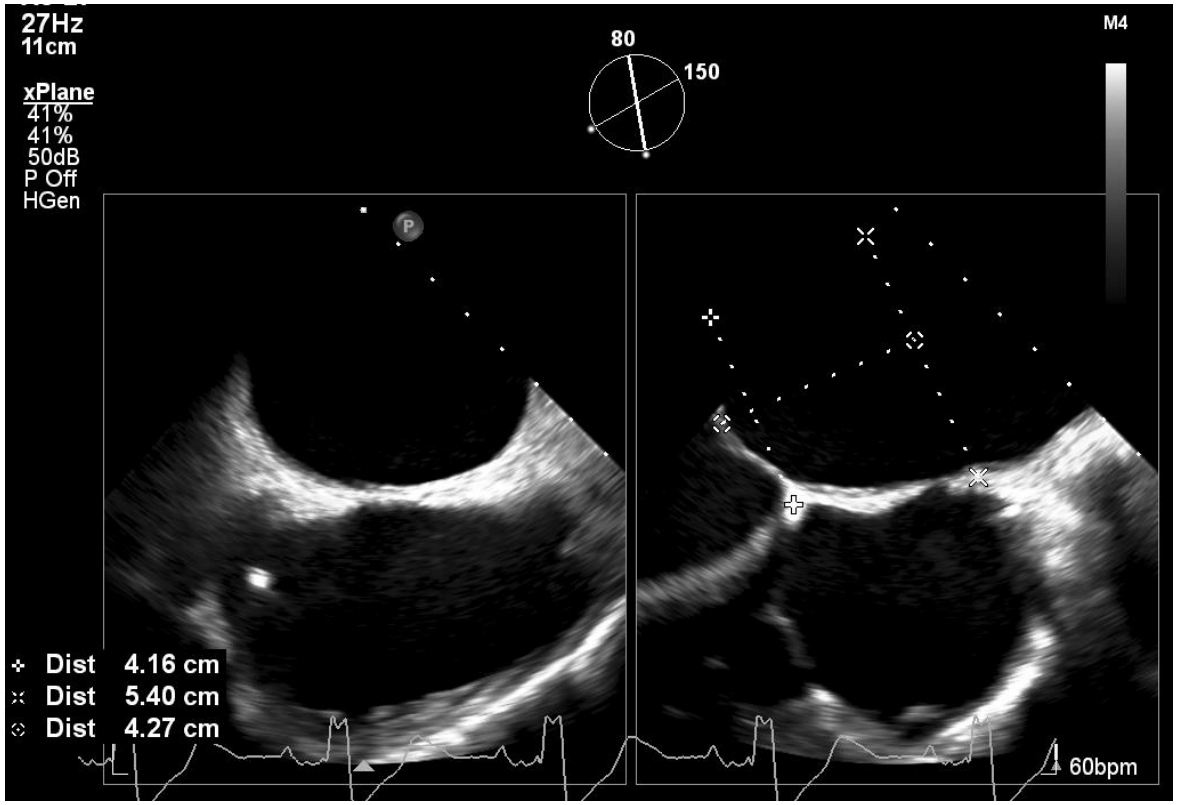
MitraClip Procedure

“Transseptal Puncture”





Puncture mid (superior)/posterior site above 40-45 mm from mitral valve annulus.

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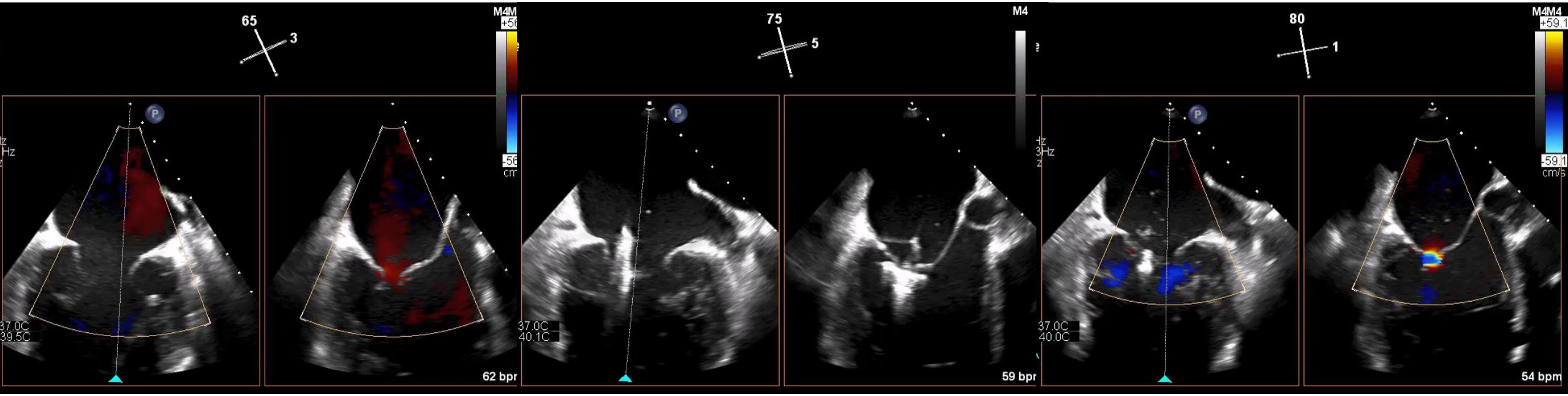
MitraClip Procedure

“1st Clip Implantation”



Deploy the 1st clip medial A2/P2. (Medial ⇒Lateral is always easy…)
MR improved from severe to moderate.
No MS and prepare the 2nd clip.

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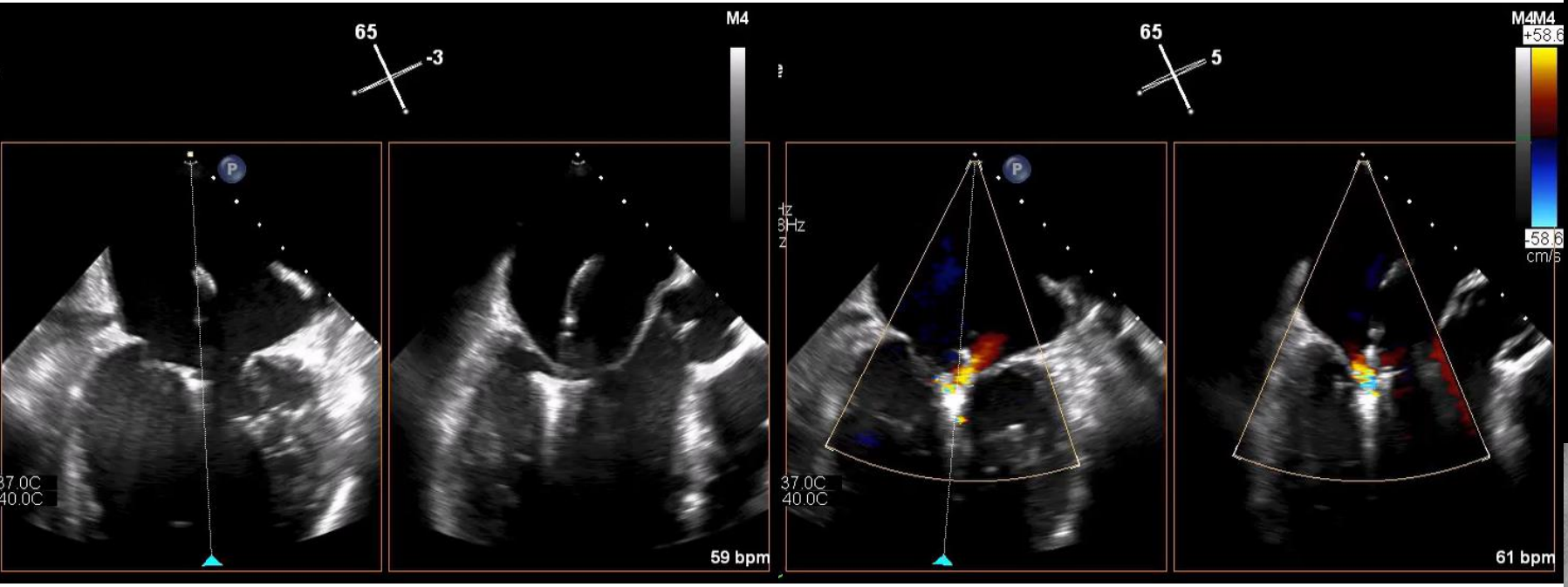
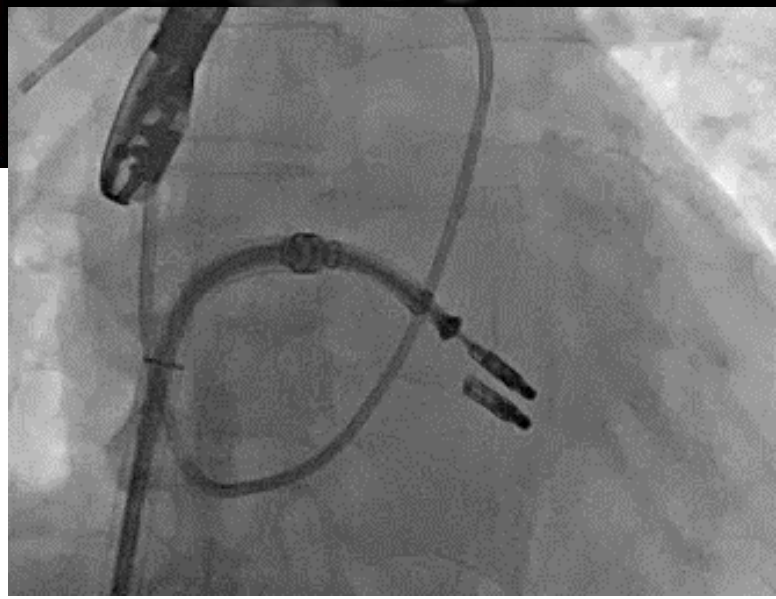
MitraClip Procedure

“2nd Clip Implantation”



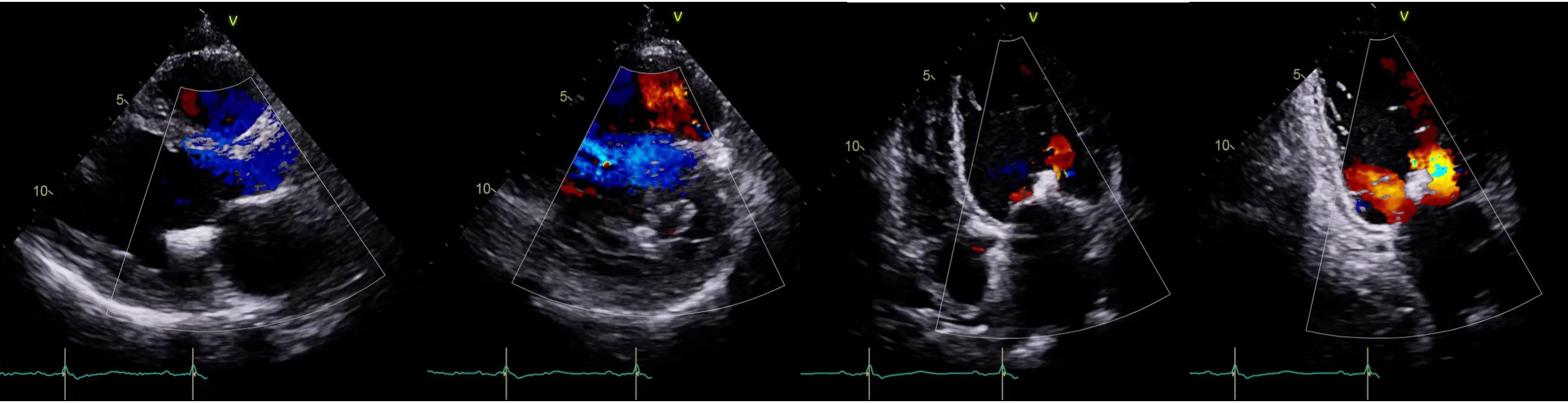


Deploy the 2nd clip just lateral to the 1st clip

MR decreased to trivial

Mean PG = 3mmHg

Follow-up TTE



Trivial- MR, MS (-), LVEF = 24%

Dyspnea and orthopnea disappeared after the procedure
Discharged 1 week after the procedure.
NYHA class I at 3 months follow-up.

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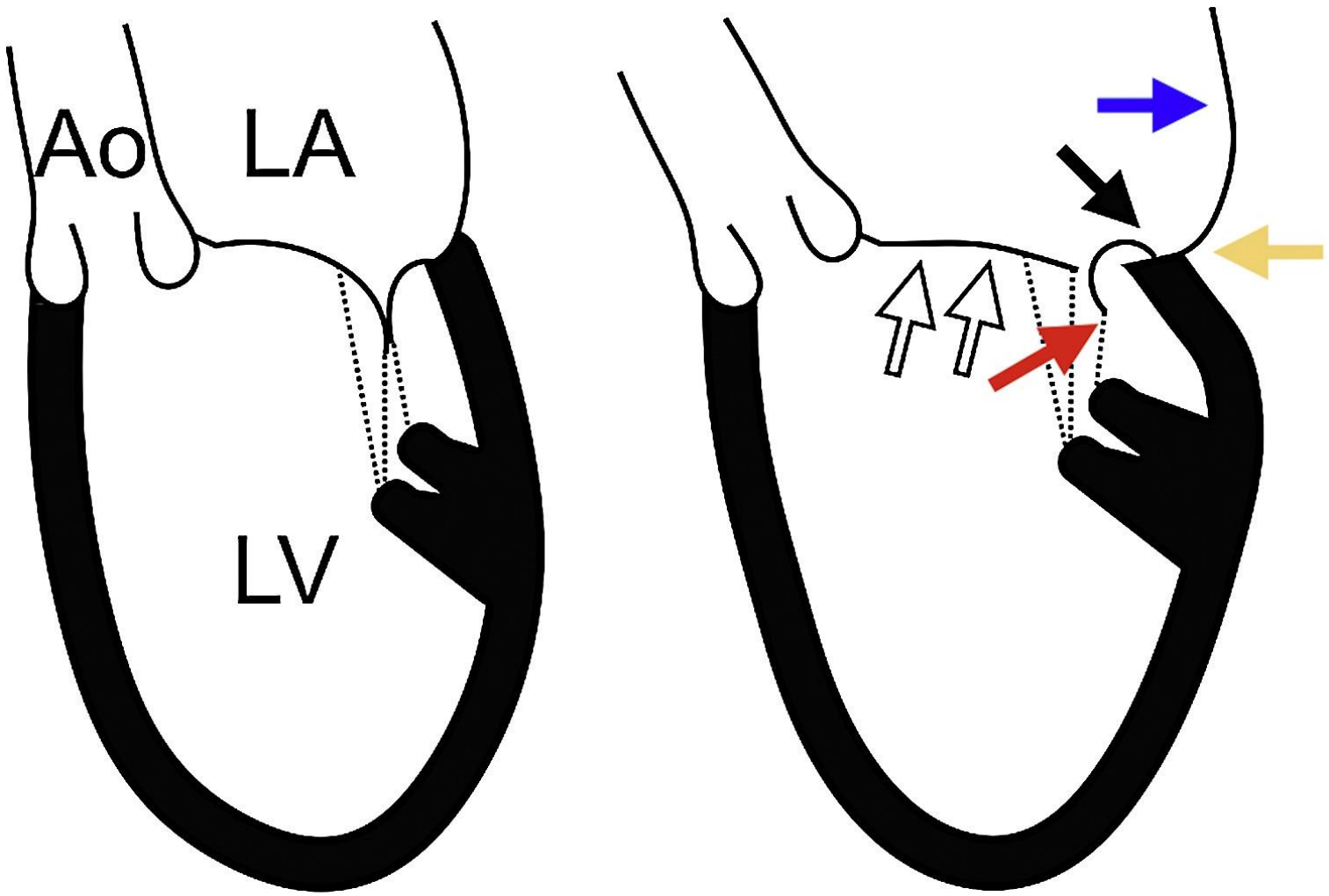
Types of Functional MR

- Ischemic MR
- Non-ischemic MR
  - DCM (Sometimes difficult due to restrictive posterior leaflet)
  - HCM (Technically easy because of sufficient leaflet length)
  - **Atrial MR (Most difficult type in functional MR)**

Hot topic in Japanese MitraClip conference !
Atrial MR more frequently observed in Japan than Western countries
No data about MitraClip for atrial functional MR

Atrial Functional MR



- The anterior mitral leaflet is flattened along the mitral annular plane with mitral annular dilation.
- The posterior wall of the LA extends behind the posterior mitral annulus with LA dilation.
- The posterior mitral annulus is displaced backward to the LA side from the crest of the posterior LV.
- The backward LA enlargement leads to the inward bending of the basal posterior LV.
- The tip of the posterior mitral leaflet is tethered toward the posterior.
- As a result, the posterior mitral leaflet curves, and its movement becomes restricted.

Ito A, et al. J Cardiol. 2017;70(6):584-590.

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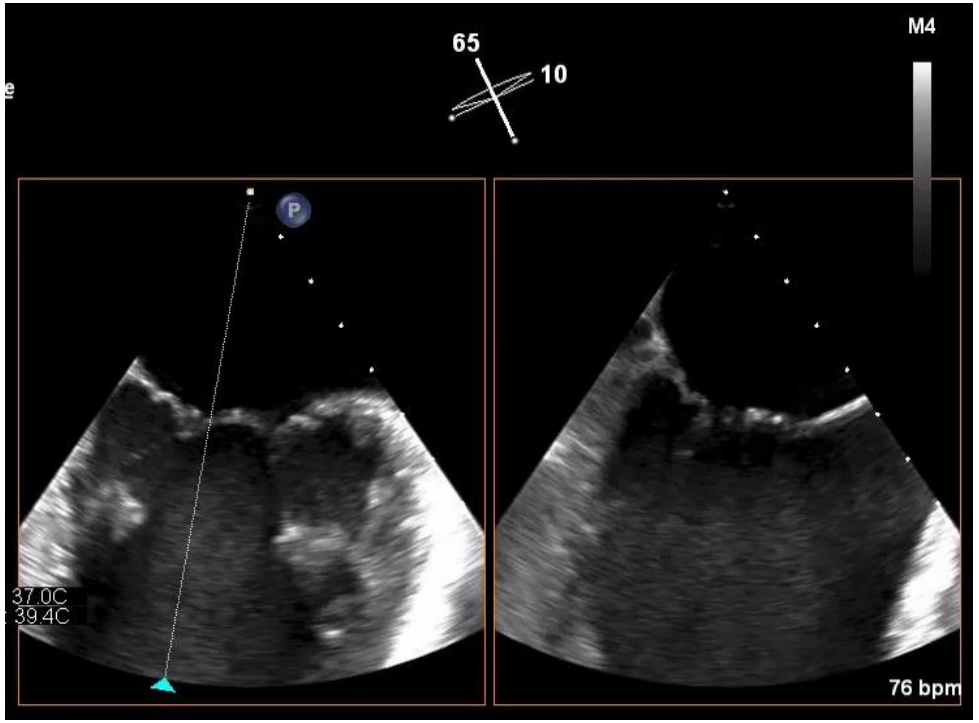
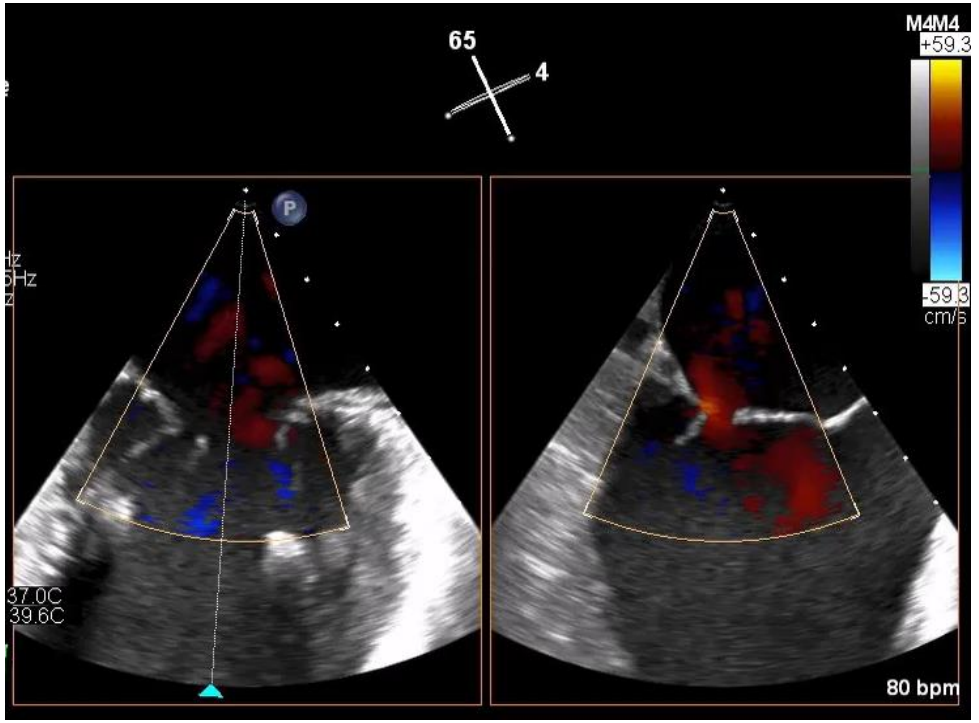
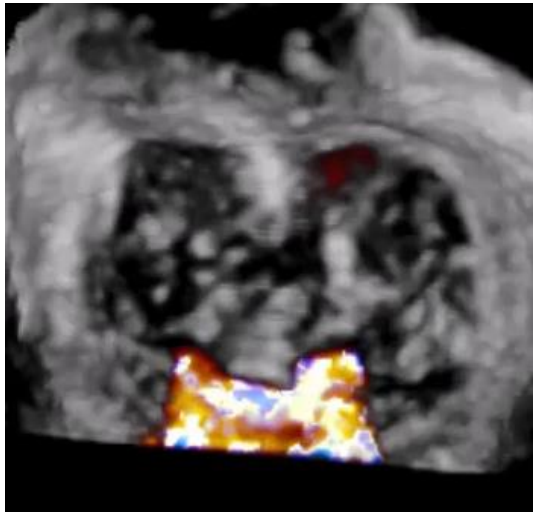
Atrial Functional MR with LV Dysfunction







Why is atrial functional MR difficult for MitraClip ?

- Short posterior leaflet
- Highly tethered posterior leaflet
- Highly mobile anterior leaflet

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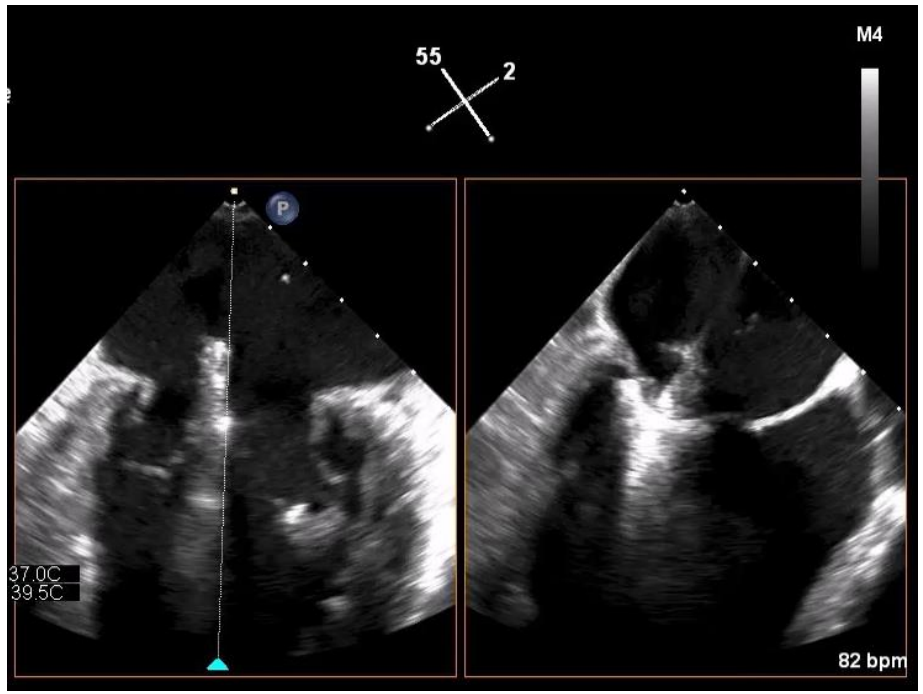
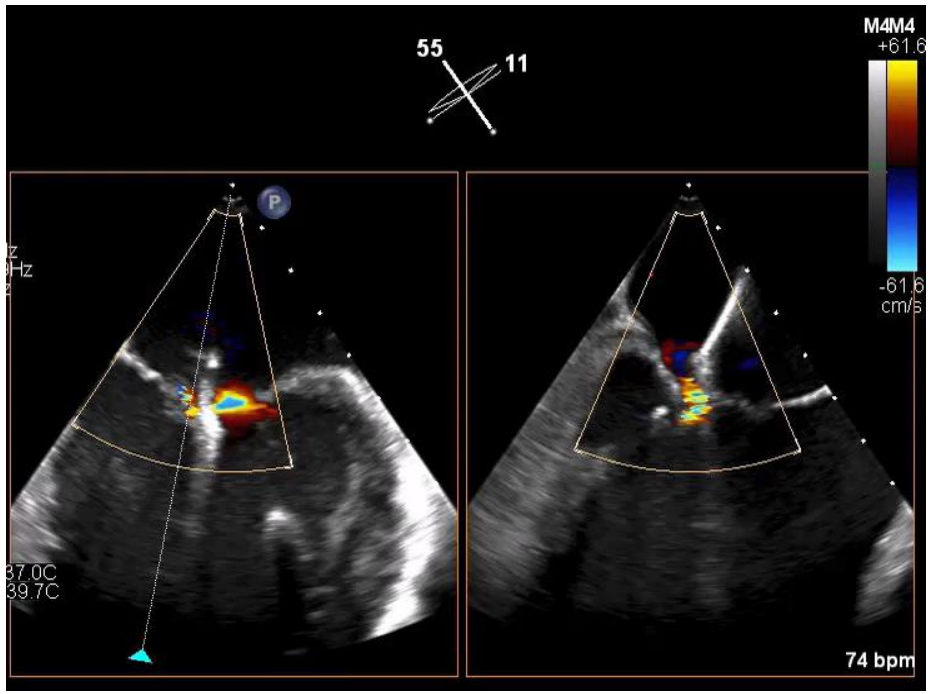
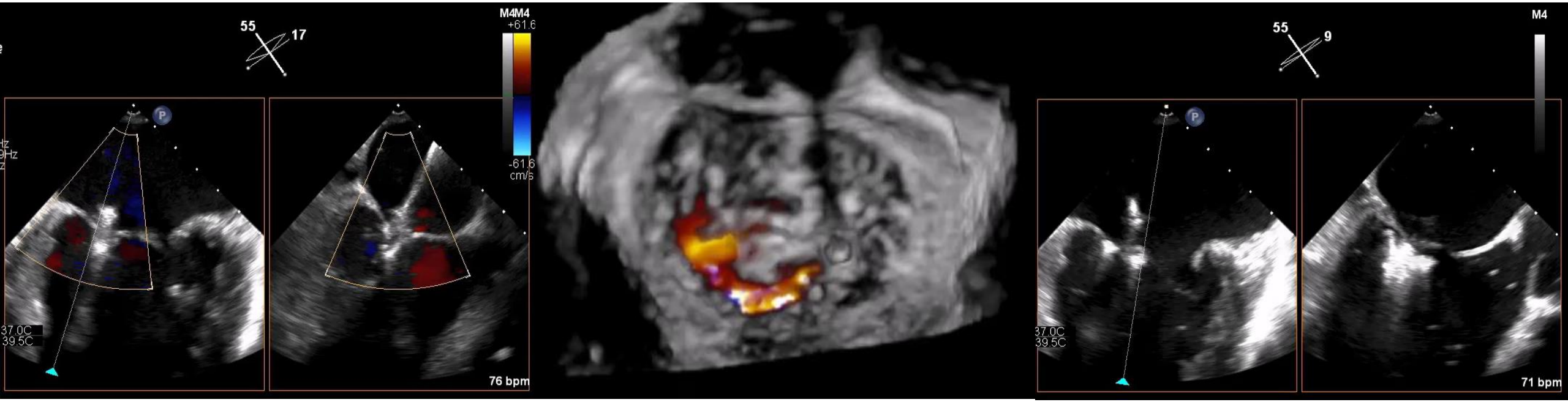
MitraClip for Atrial Functional MR

- Transseptal puncture is always easy, but puncture point is different because LA is extremely huge.
- MR reduction is not so dramatic probably due to the residual PML tethering.





Modified Zipping Technique for Atrial MR



- According to the “modified zipping technique”, 1st clip is implanted at most medial site of MR jet to disappear residual MR medial to the clip.
- Then, 2nd clip should be implanted at the center of residual MR.
- In order to improve tethering angle, clip is maximally pulled up the posterior leaflet.

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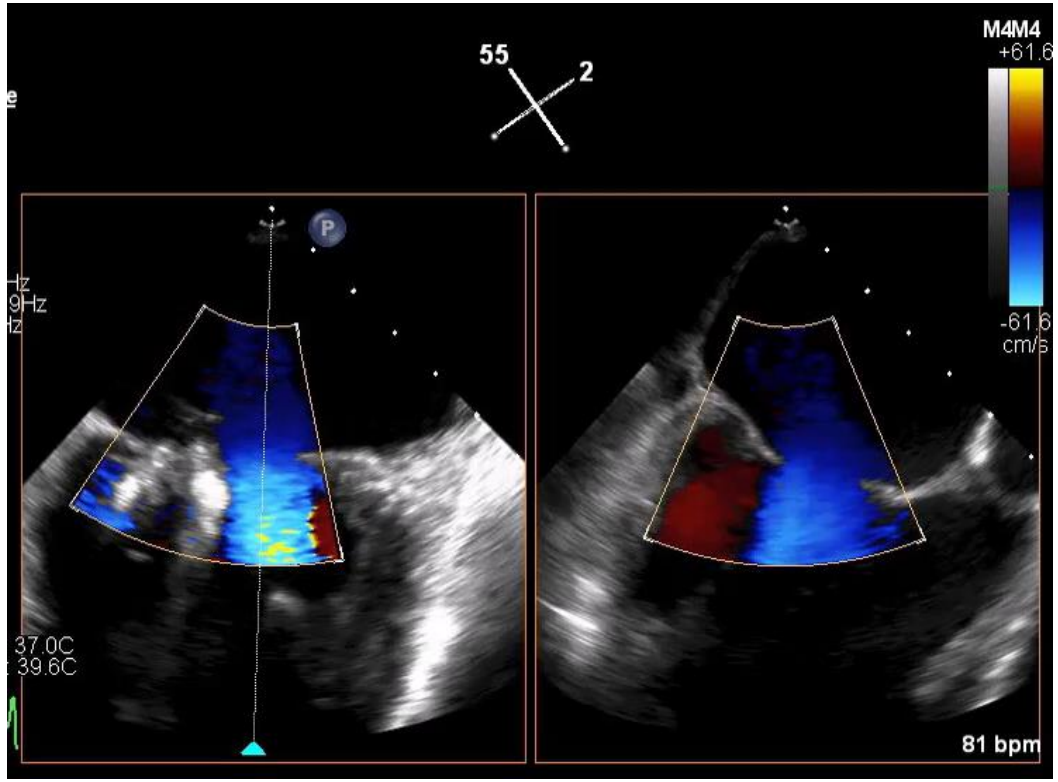
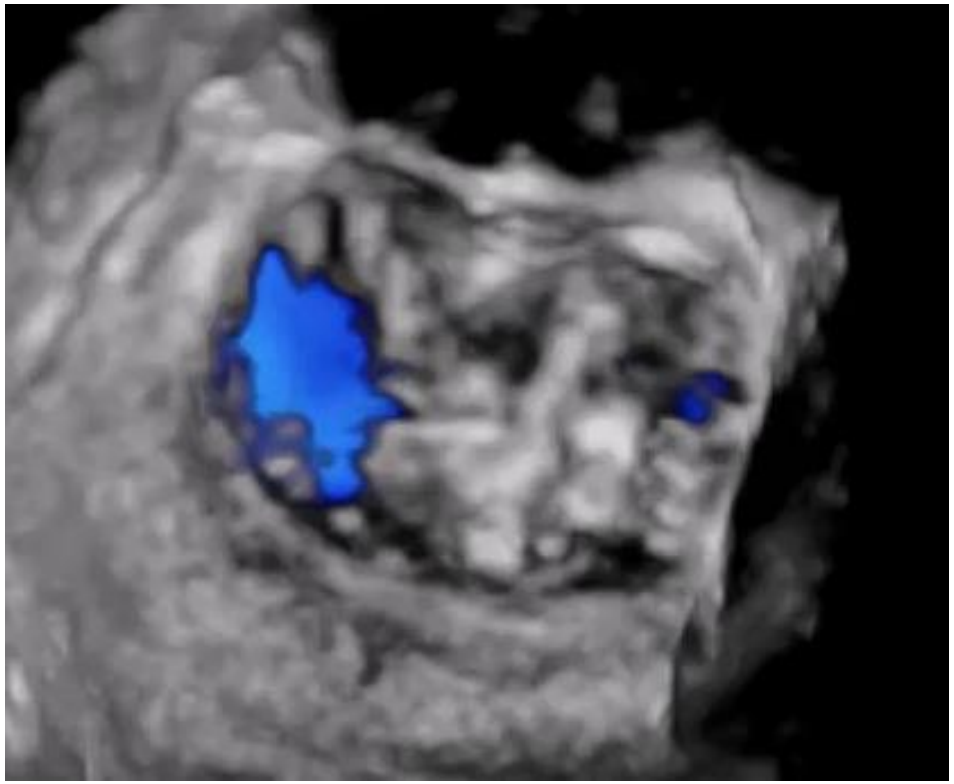
MitraClip for Atrial Functional MR





- MR reduced from severe to mild-moderate.
- Particularly, the direction of residual MR jet changed from eccentric to central jet.
- This strategy can be effective this atrial functional MR.

Pt Screening in Japanese (Asian?) Population

- So many atrial functional MR in the screening steps
  - The shape of LA in persistent AF patients are different from Western people ?
- Coexisting severe TR (especially in atrial MR)
  - Unfavorable effect of severe TR
  - Necessity of iatrogenic ASD closure for right-to-left shunt
- Small left atrium (due to small body size ?)
  - Difficult to secure the height from mitral annulus to tenting at septal puncture
- Small mitral valve area (due to small body size ?)
  - Risk of mitral valve stenosis
- Leaflet tear during/after the procedure
  - More frequently reported than Western countries

Summary

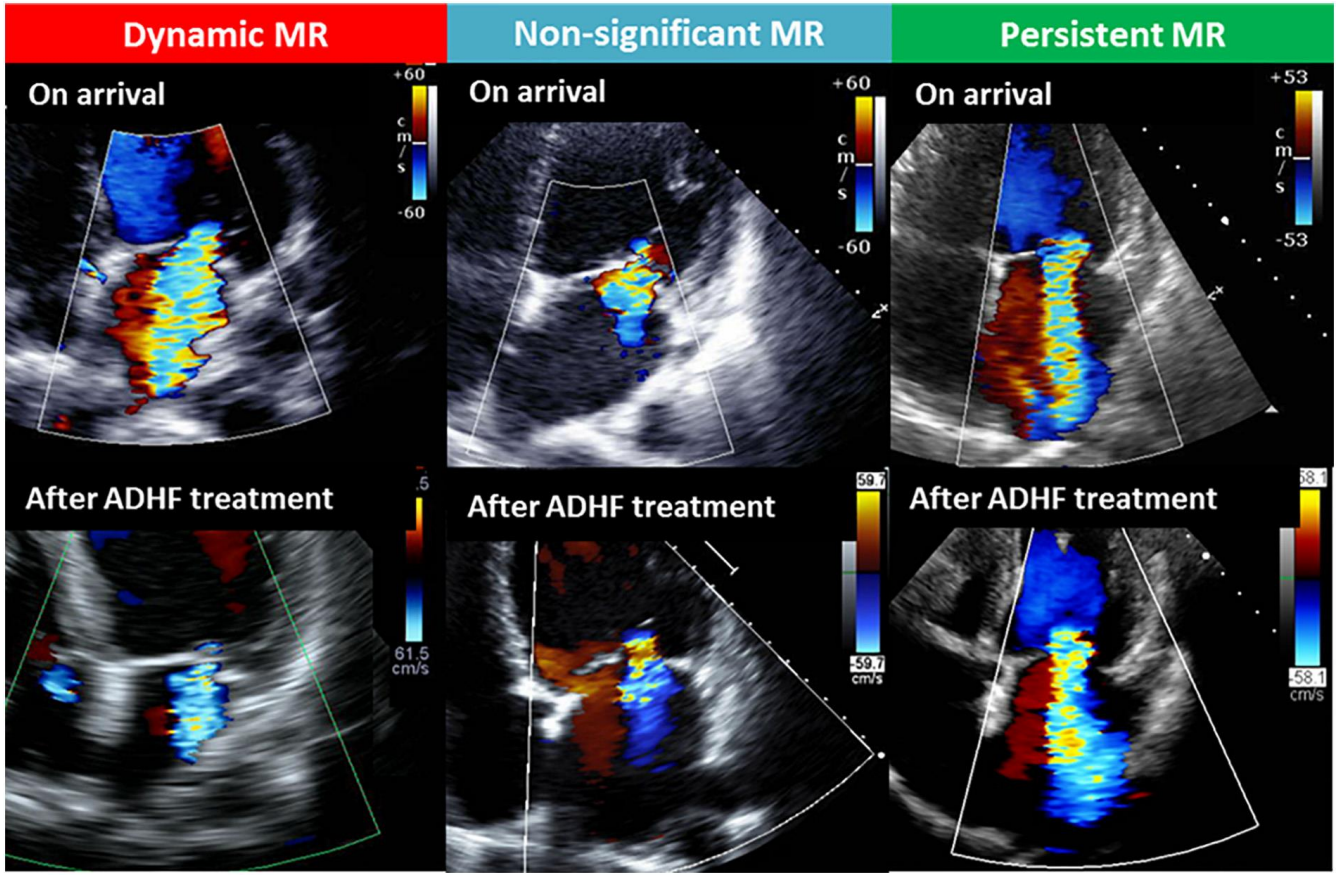
- MitraClip just started in Japan for high surgical risk patients with severe MR this year.
- Initial results were safe and favorable in functional MR patients.
- Beyond the COAPT experience, various MR types among functional MR can be a therapeutic target for the MitraClip.

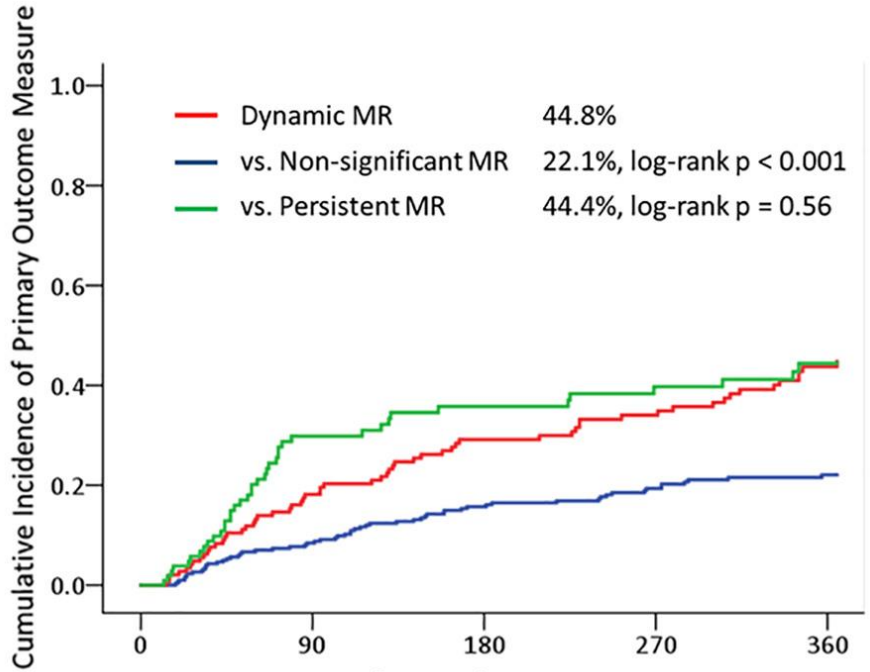
Dynamic MR and Heart Failure

Dynamic severe mitral regurgitation on hospital arrival as prognostic predictor in patients hospitalized for acute decompensated heart failure

Shunsuke Kubo *, Yuichi Kawase, Reo Hata, Takeshi Maruo, Takeshi Tada, Kazushige Kadota

Department of Cardiology, Kurashiki Central Hospital, Kurashiki, Japan





No. at risk			
Dynamic MR	149	94	57
Non-significant MR	308	223	155
Persistent MR	106	53	34

Adjusted Risks for Primary Outcome Measure

	Adjusted HR (95% CI)	P value
Dynamic MR	Reference	
Non-significant MR	0.50 (0.34-0.73)	<0.001
Persistent MR	1.08 (0.69-1.67)	0.75

Kubo S, et al. Int J Cardiol. 2018;273:177-182.

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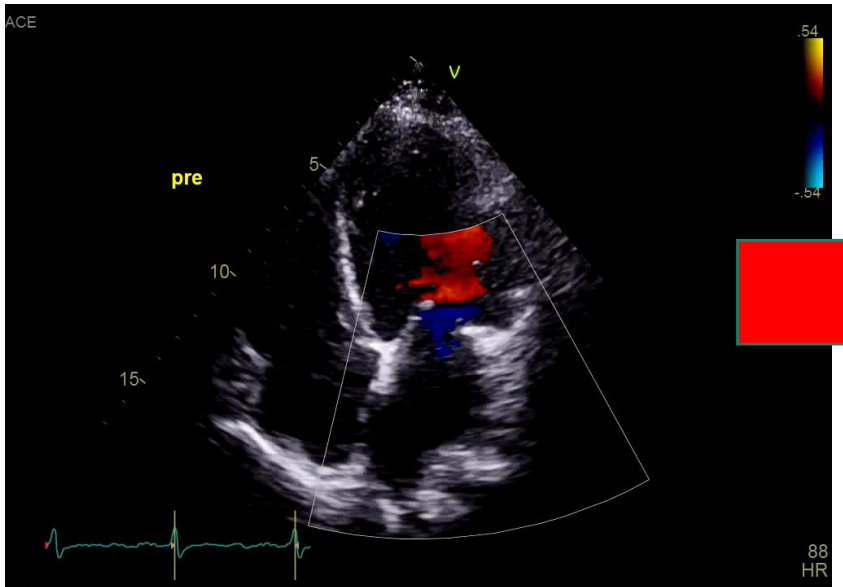
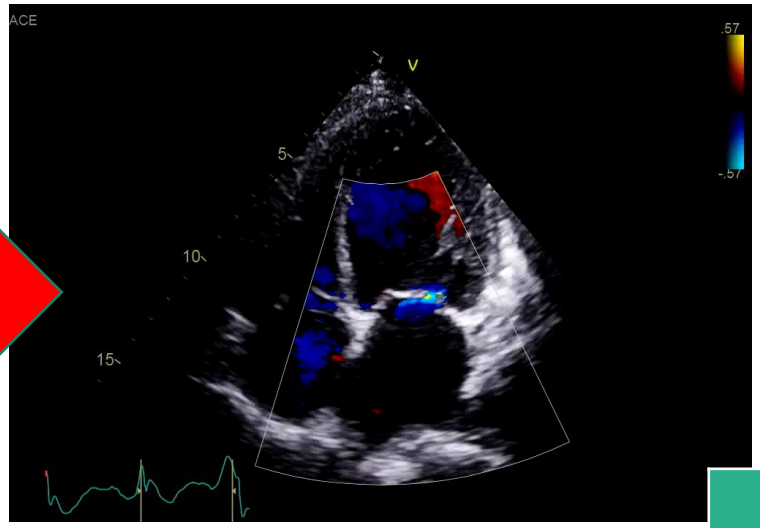
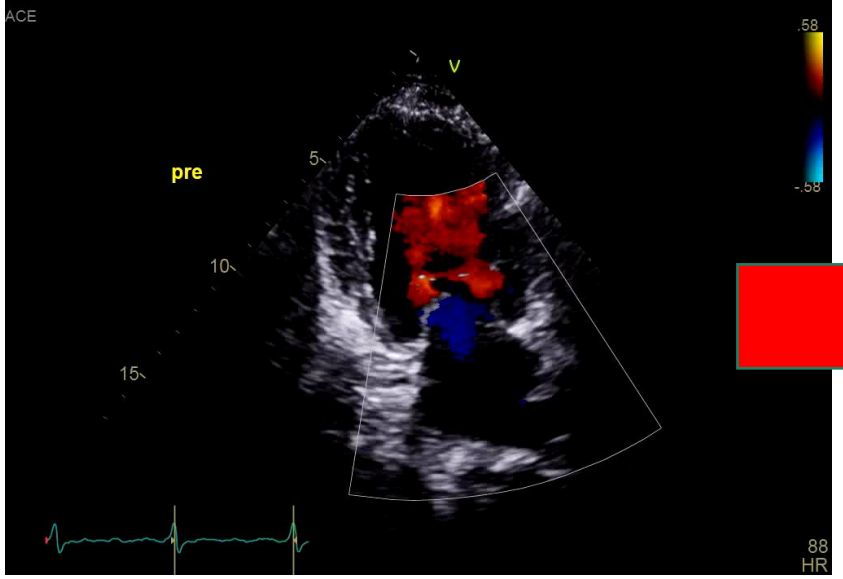
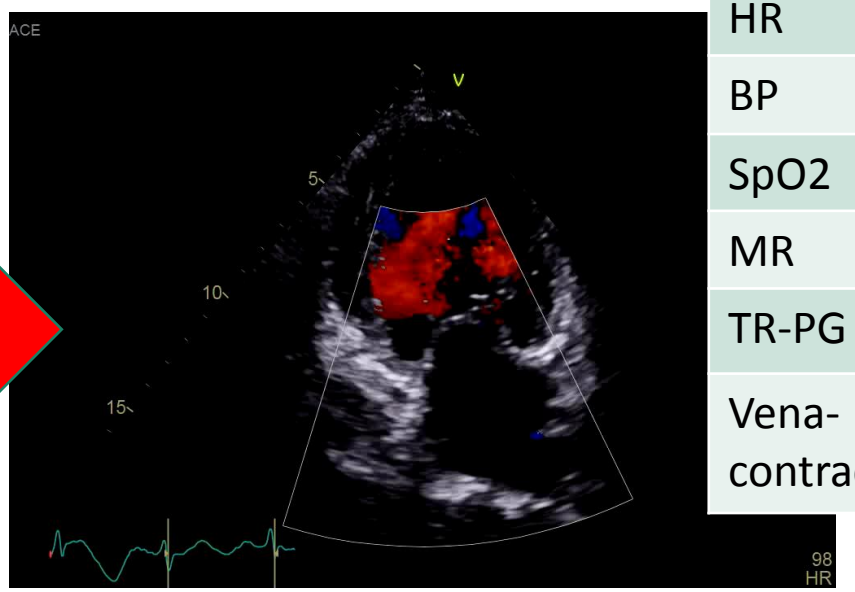
64 Years Female, Ischemic Cardiomyopathy
Multiple times HF Hospitalization









[Exercise Stress]
20W 3 min
Dyspnea Stress

	0W	20W
HR	96bpm	100bpm
BP	77/58mmHg	99/64mmHg
SpO2	98%	97%
MR	moderate	severe
TR-PG	22mmHg	36mmHg
Vena-contracta	6.4 × 7.1mm (mean 6.75)	10 × 15mm (mean 12.5)

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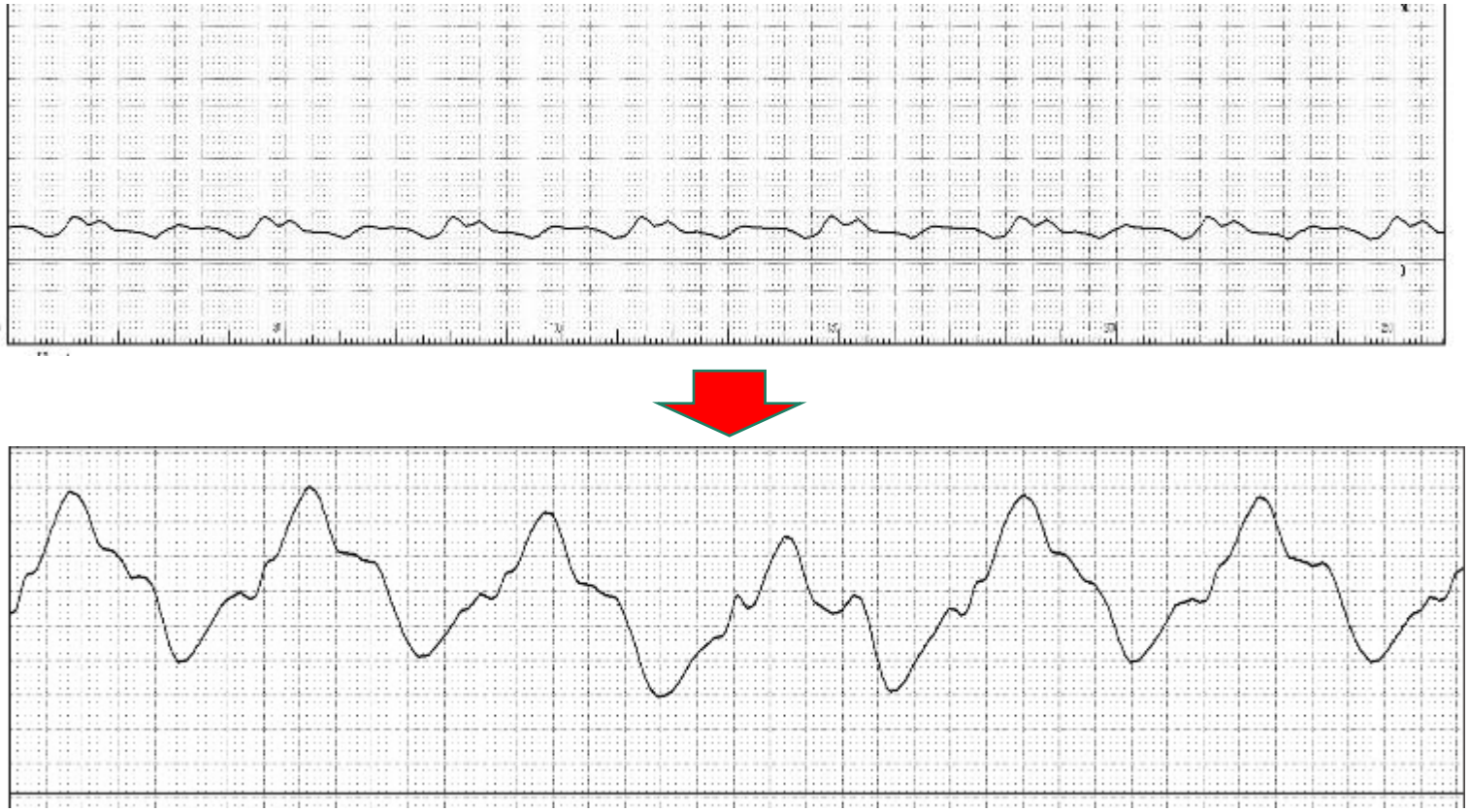
Right Heart Catheterization

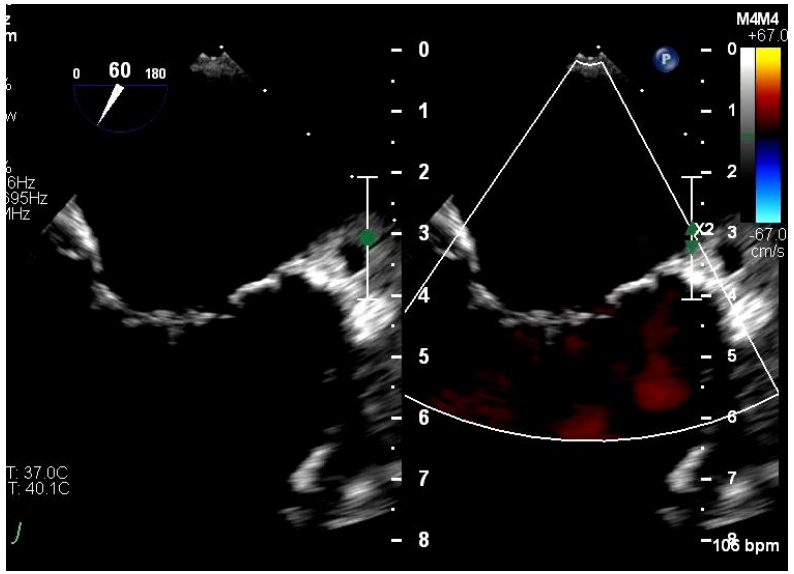


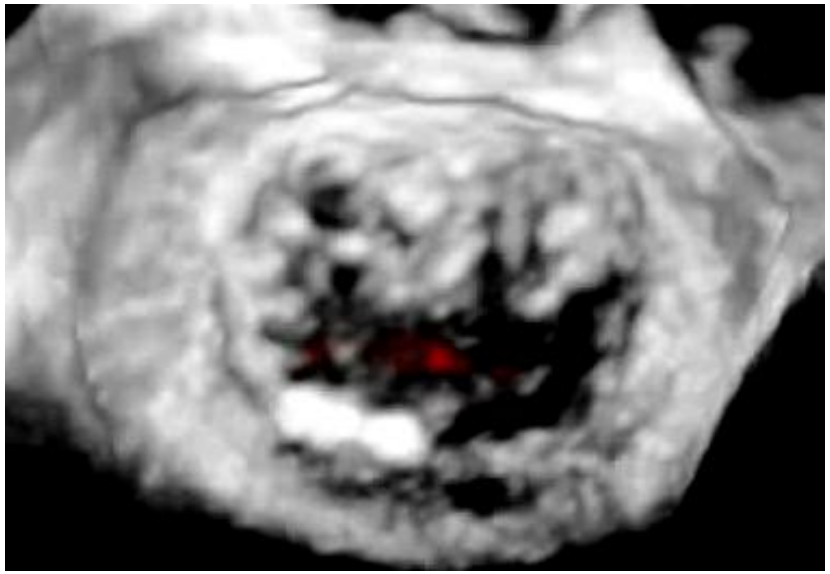
【Hand-Grip Stress】
PA increases.
PCWP, especially v-wave, increases.
↓
Worsened MR will affect HF hospitalization !

	Pre Stress	Post Stress
PA (mmHg)	18/16/15	40/19/28
PCWP (mmHg)	9	21

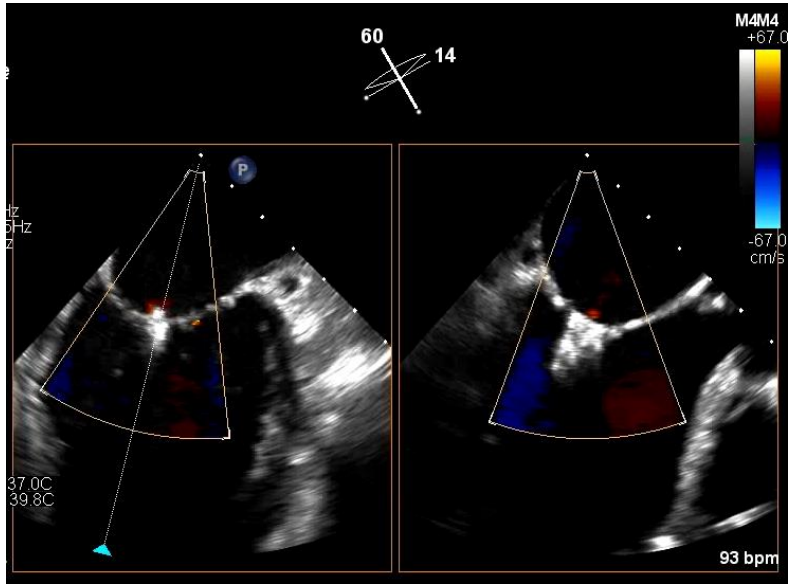
MitraClip Procedure

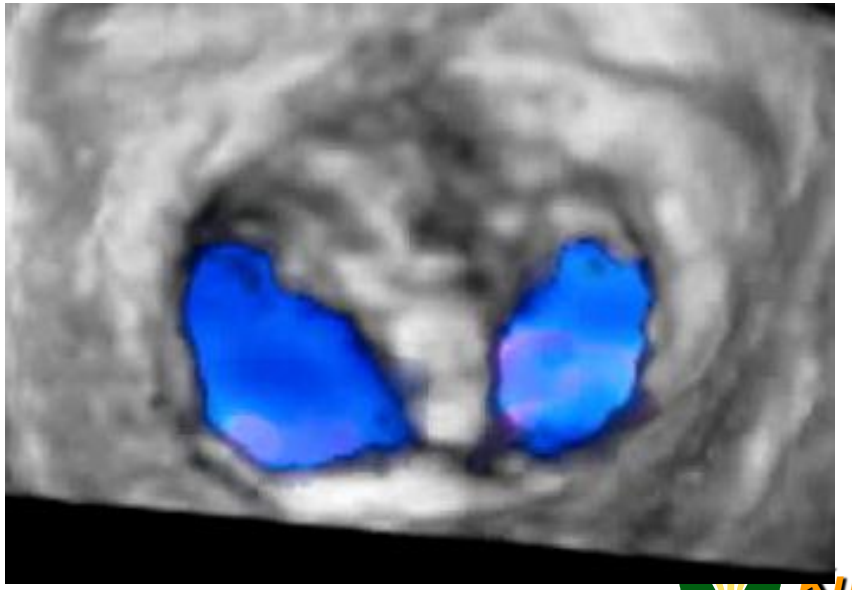
Pre





Post





Procedure time:
66 min
Trivial MR

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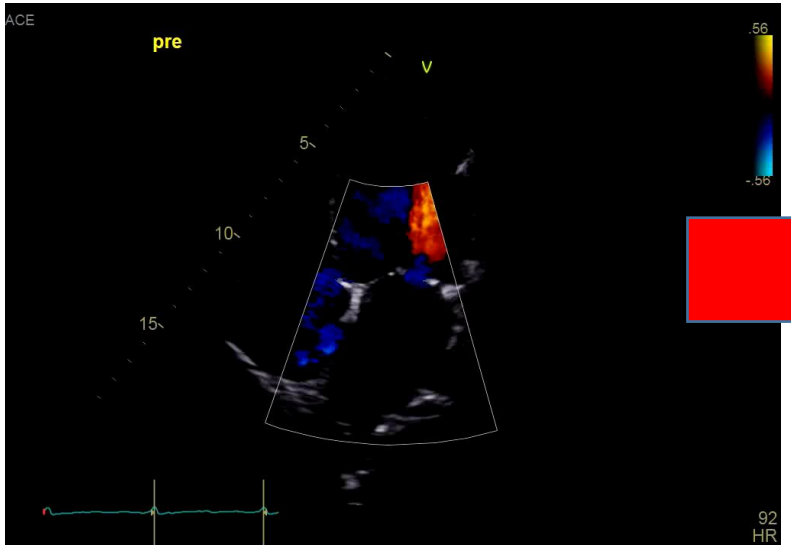
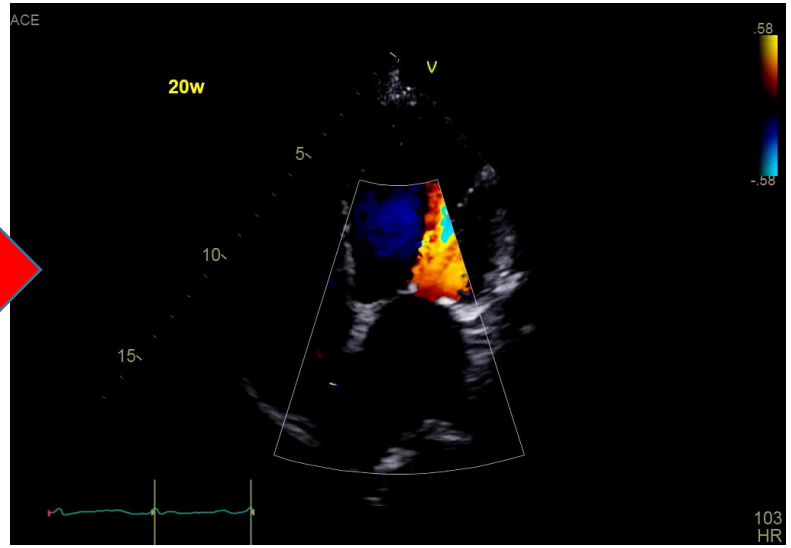
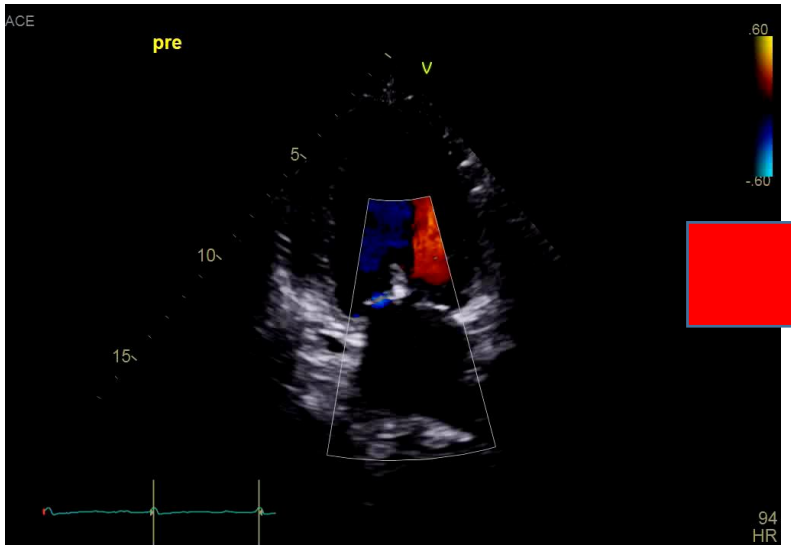
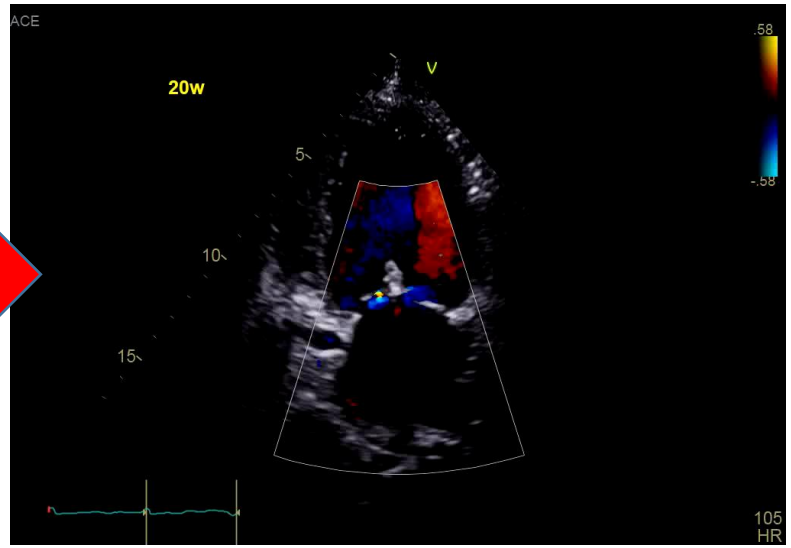
Follow-up Exercise Stress TTE





	0W	20W
HR	96bpm	108bpm
BP	94/68mmHg	99/64mmHg
SpO2	96%	99%
MR	trivial	trivial
TR-PG	22mmHg	33mmHg





NYHA 1-2 symptoms
No hospitalization after the procedure

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