Percutaneous Mitral Valve Interventions: Contemporary Update

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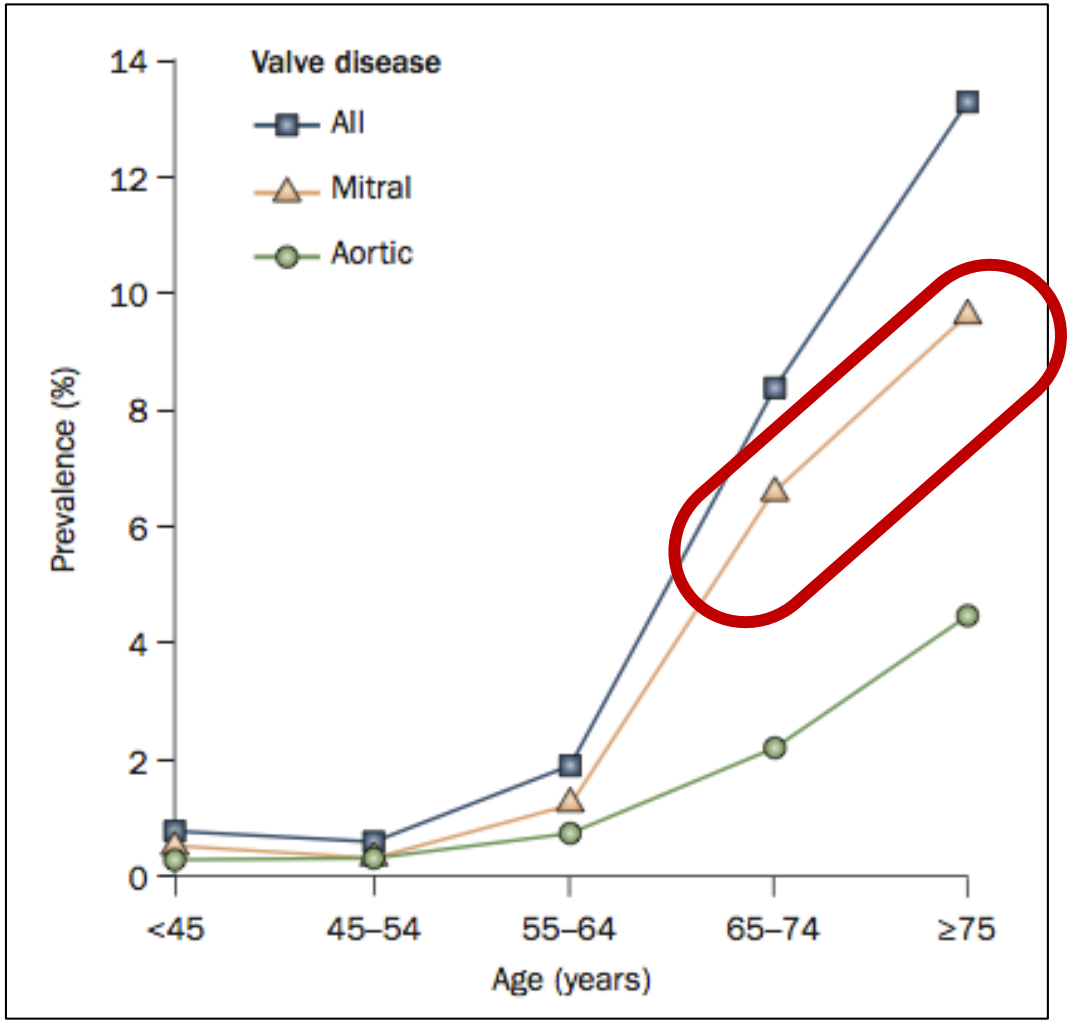
DISCLOSURES

- Proctor for Edwards Lifesciences

Prevalence
Moderate-Severe Valvular Disease



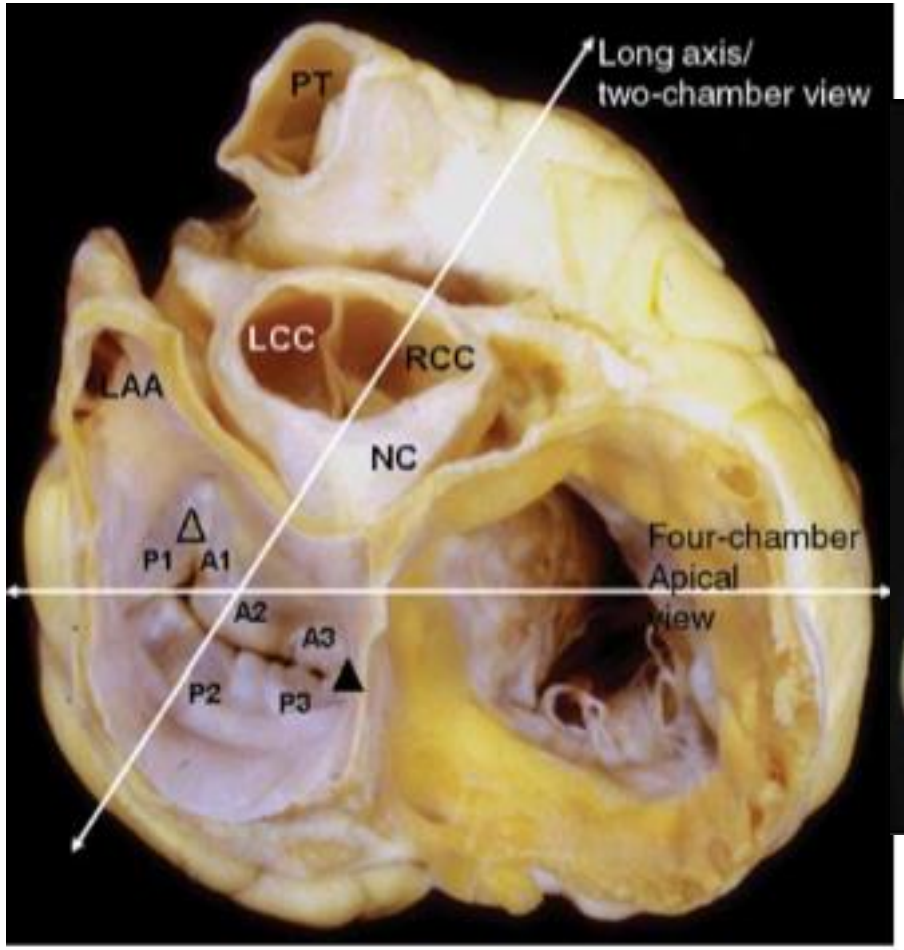
Nkomo et al. Lancet 2006;368:1005-11.

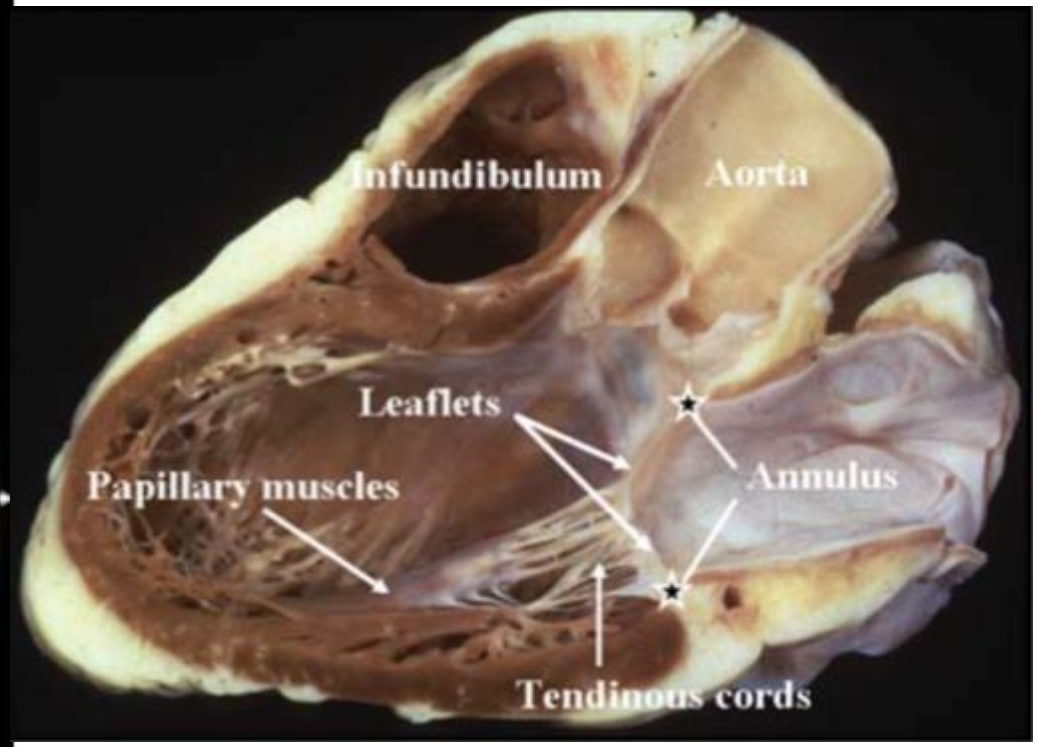
Mitral Regurgitation Undertreated

	All patients (n=1294)	Ejection fraction <50% (n=538)	Ejection fraction ≥50% (n=756)
Mitral surgery			
Total	198 (15%)	28 (5%)	170 (22%)
Repair	149 (12%)	18 (3%)	131 (17%)
Replacement	49 (4%)	10 (2%)	39 (5%)
Tissue	23 (2%)	3 (<1%)	20 (3%)
Mechanical	26 (2%)	7 (1%)	19 (3%)

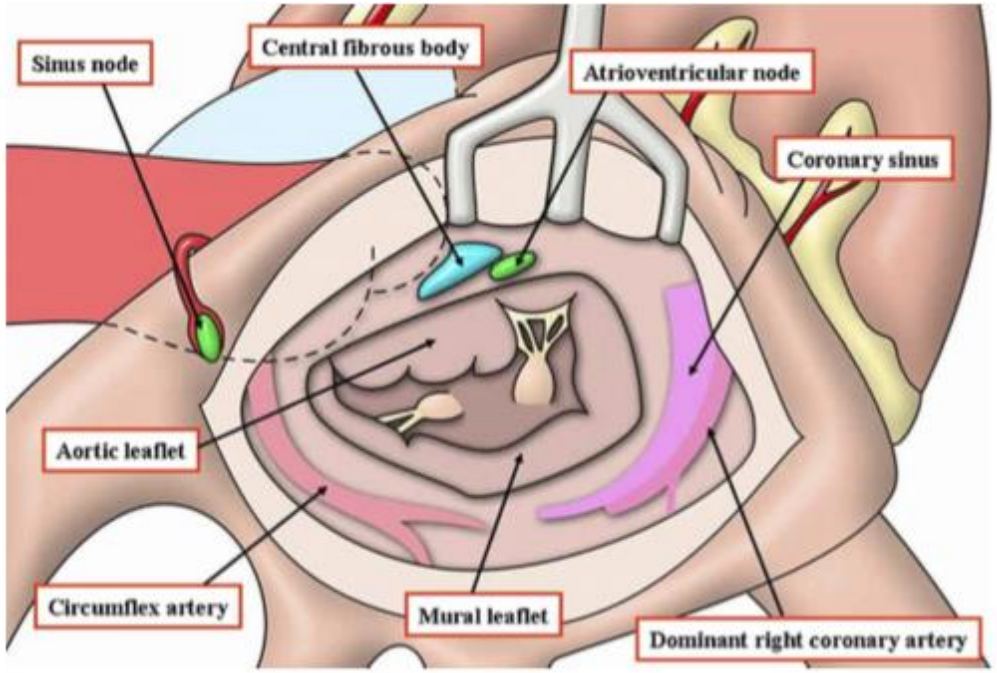
Dziadzko, V. et al. Lancet 2018;391:960-69.

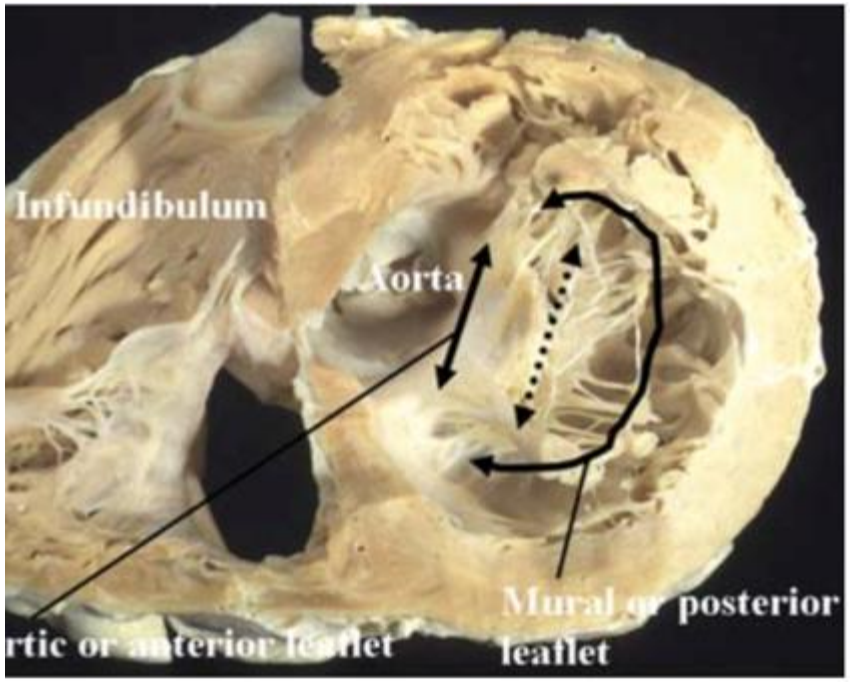
Mitral Valve Anatomy



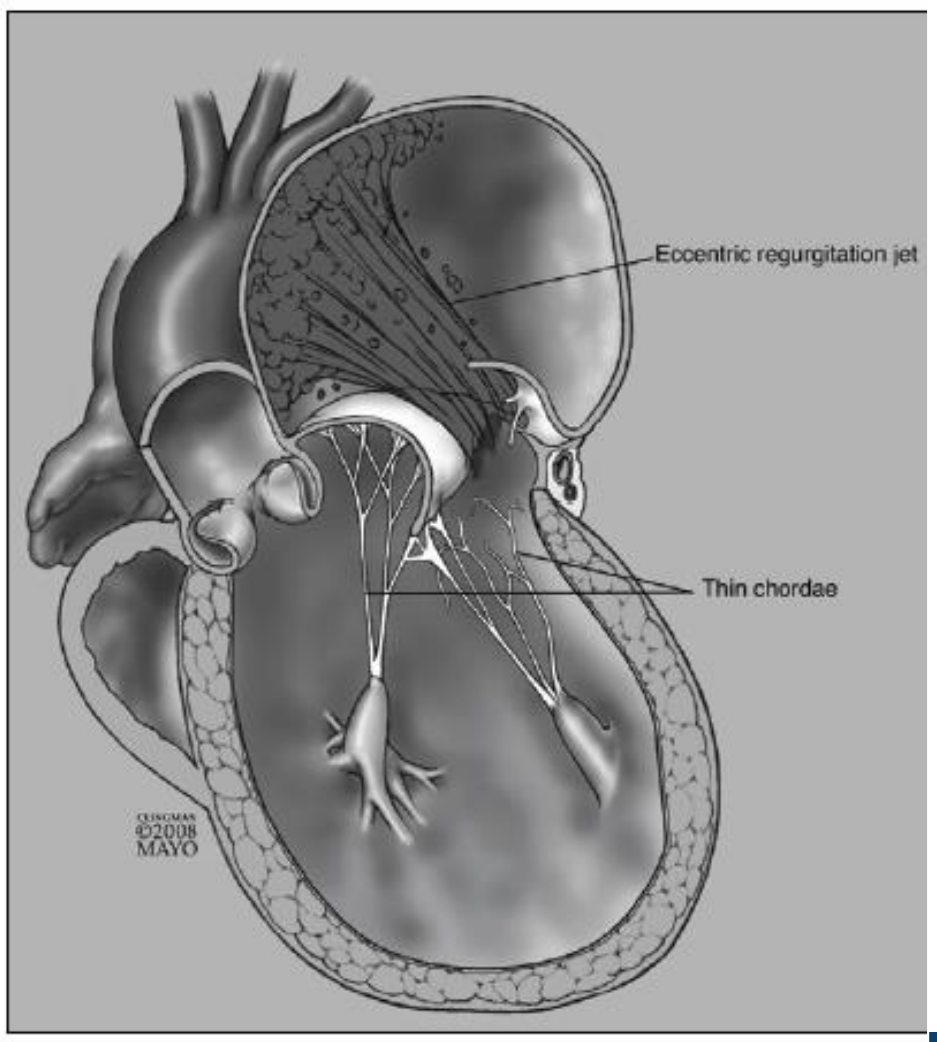


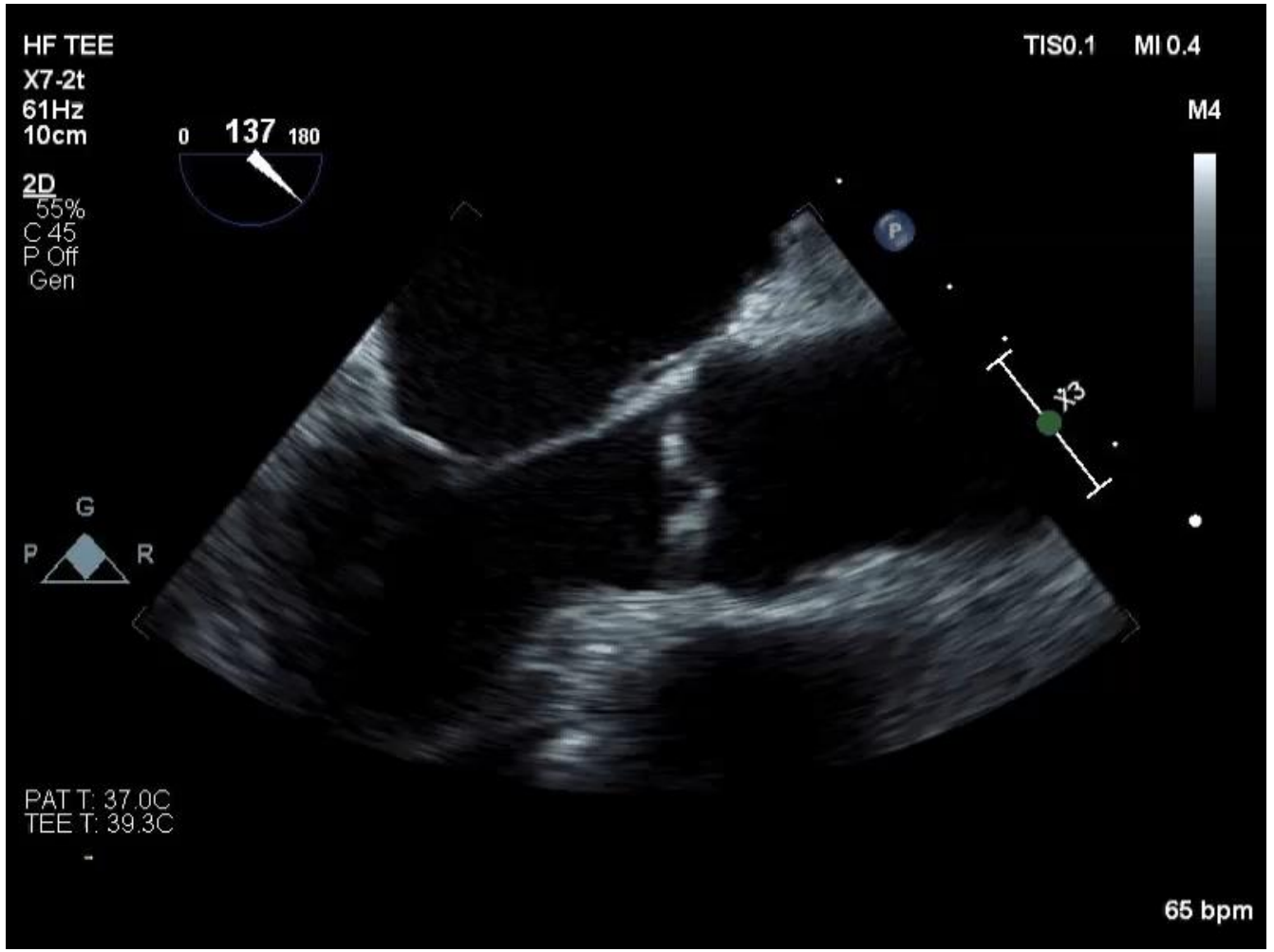
Opportunities and Challenges



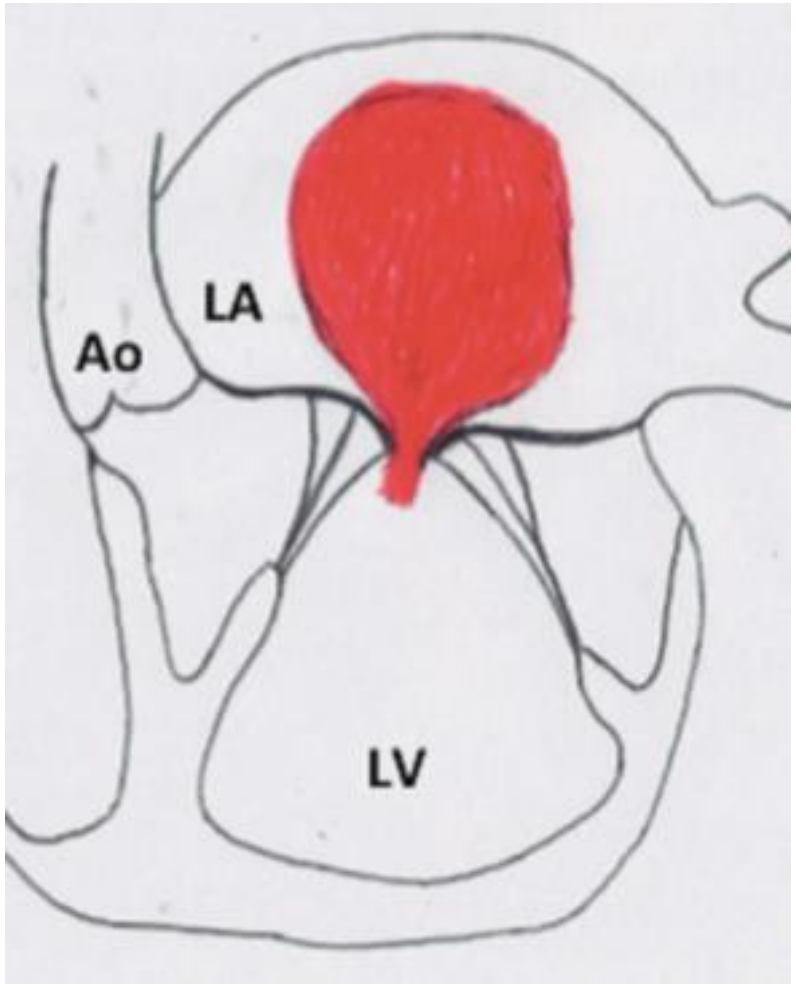


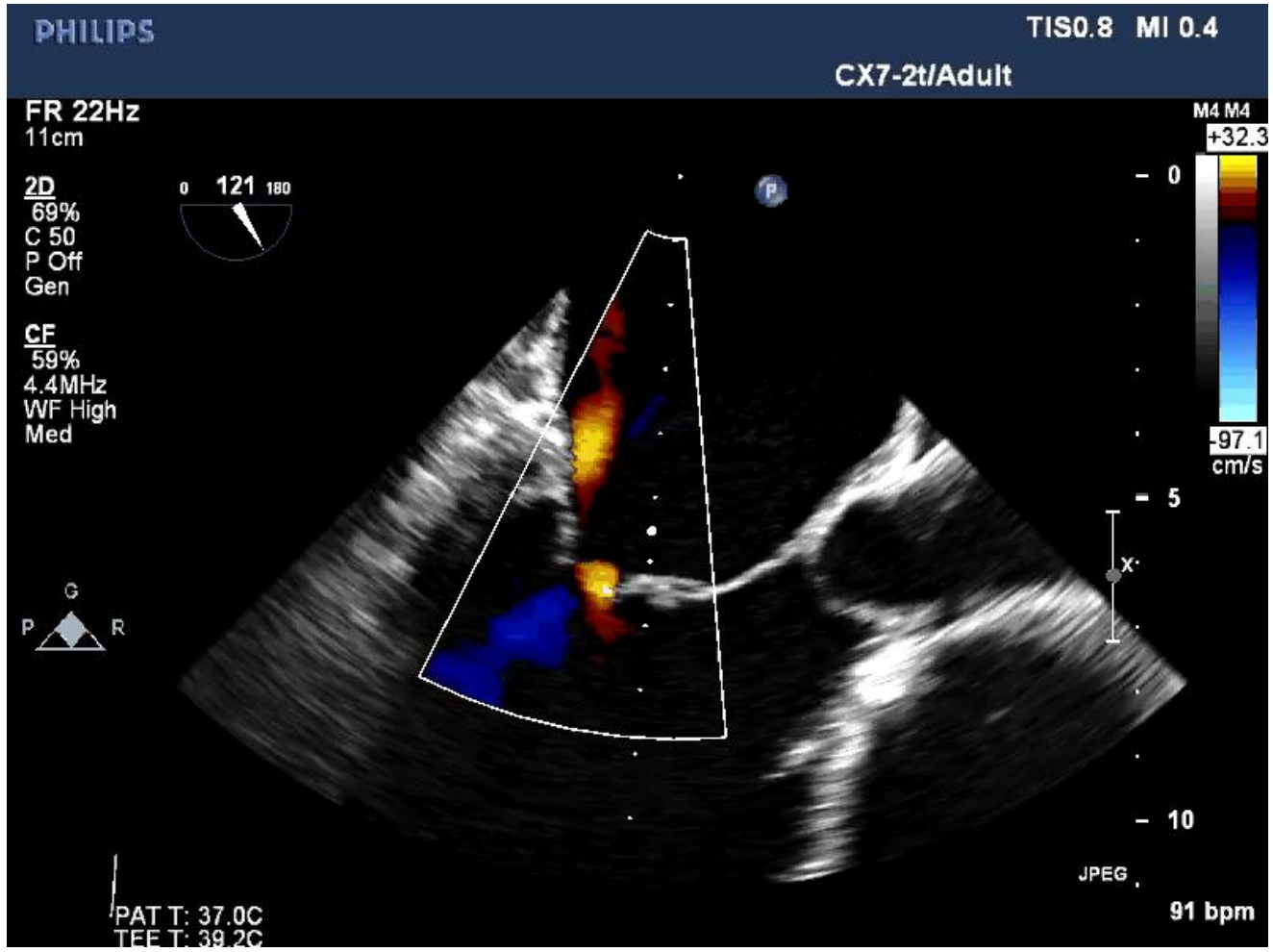
Degenerative Mitral Regurgitation
Valve is the problem



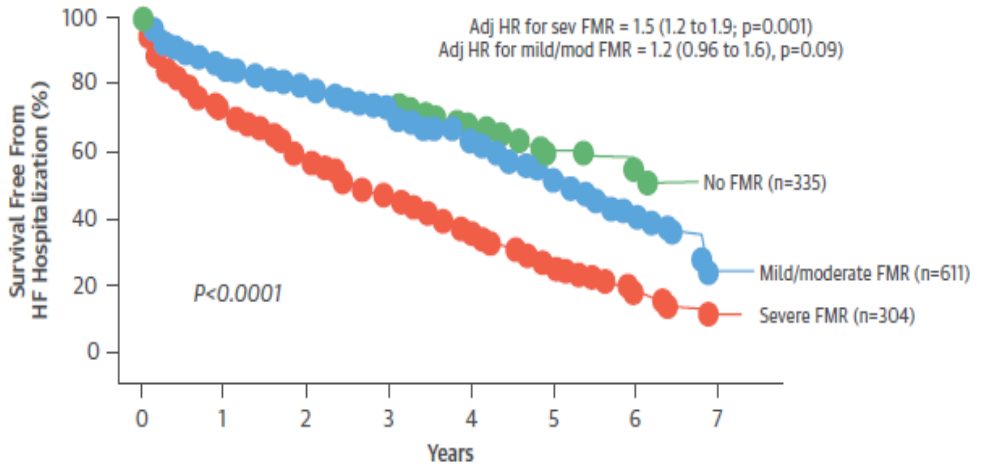


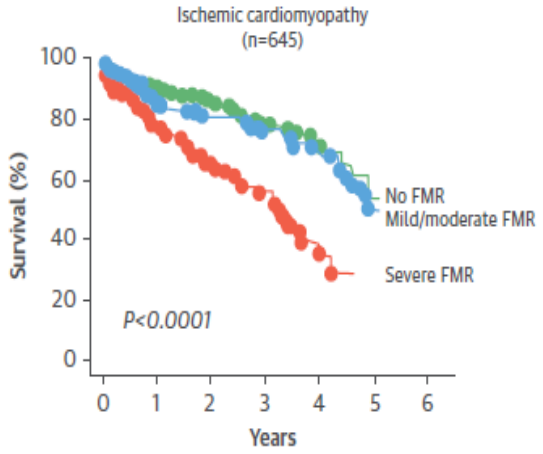
Functional MR
Muscle is the 1° disease

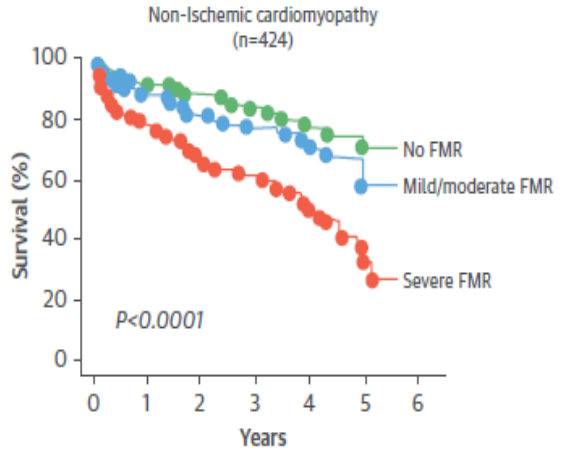




Survival in Cardiomyopathy Proportional to MR



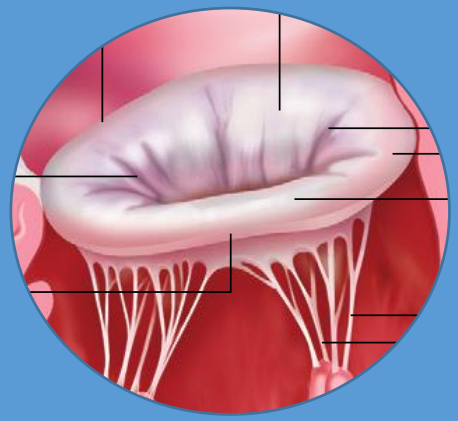




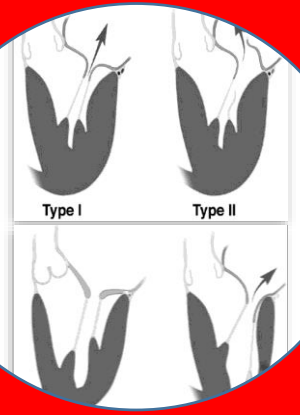
Rossi A. et al. Heart 2011;97:1675-1680.

Factors for deciding treatment

Anatomy



Function



Etiology

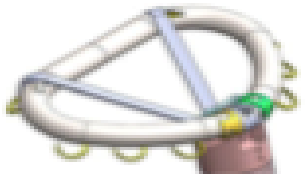
MitraClip (Abbot Vascular)
Edge-to-edge repair

NeoChord (NeoChord DS1000)
Chordal repair

V-Chordal-Off Pump (Valtech)
Chordal repair

CARILLON (Cardiac Dimensions)
Indirect Annuloplasty

ValCare MV Repair (ValCare)
Direct annuloplasty



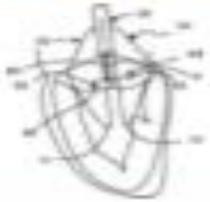
GDS Accucinch (GDS)
Direct Annuloplasty

Mitralign Bident (Mitralign)
Direct annuloplasty

Cardioband TF (Valtech)
Direct annuloplasty

Millipede Ring (Millipede)
Direct annuloplasty

Cardica Mitral Repair (Cardica)
Edge-to-edge repair



Mitra-Spacer-Transapical (Cardiosolutions)
Enhanced coaptation

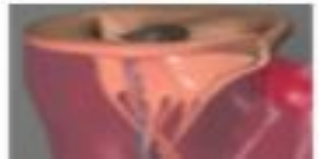
MISTRAL (Mitralix)
Chordal repair

V-Chordal-Transfemoral (Valtech)
Chordal repair

Kardium MR (Kardium)
Direct annuloplasty

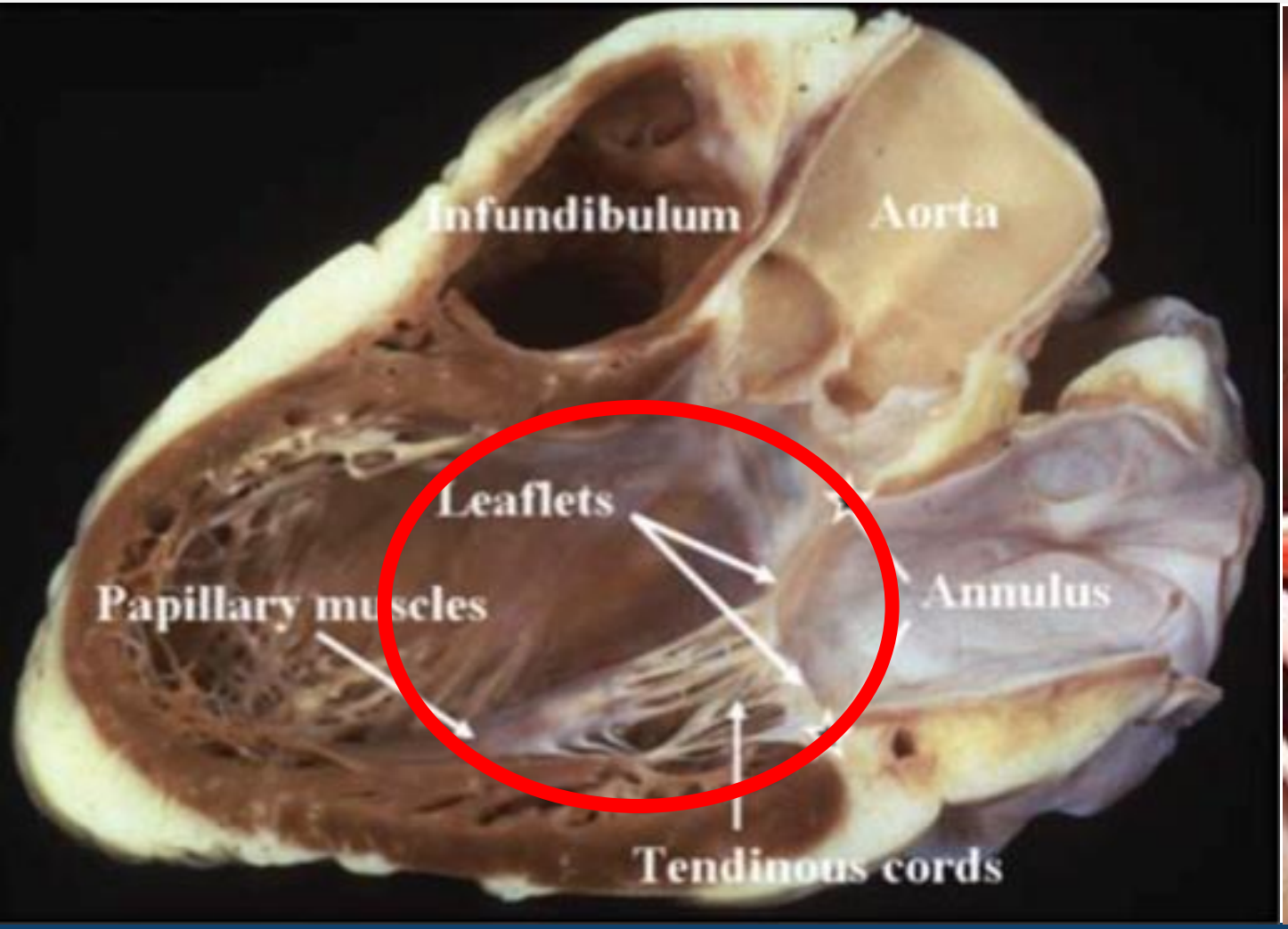
PS3 (MVRx)
Annuloplasty

MitraFlex (TransCardiac)
Edge-to-edge

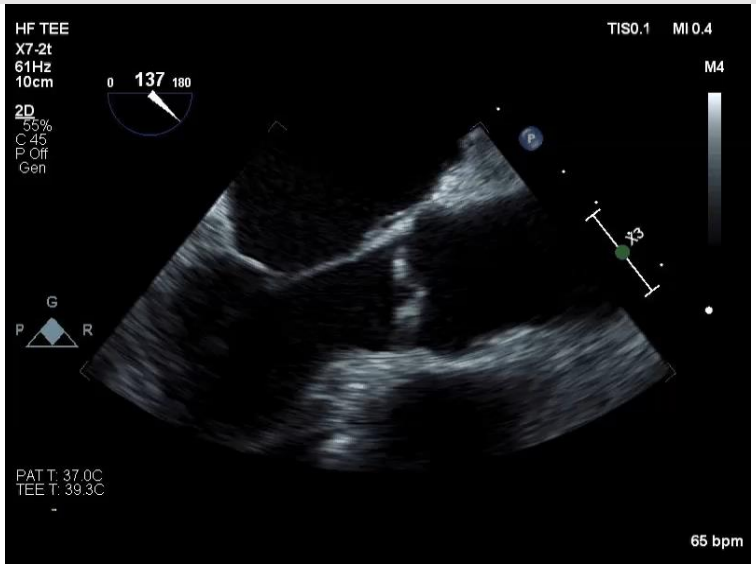


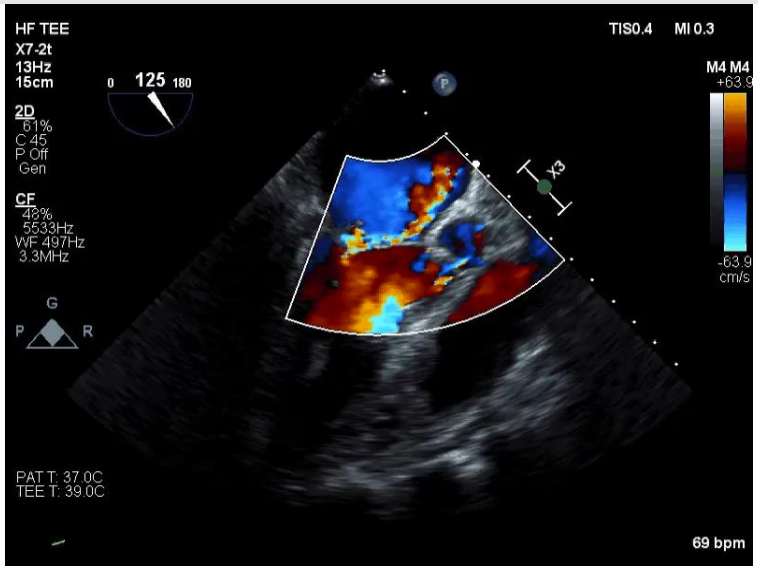
Maisano F et al. EHJ 2015;36:1651-1659.

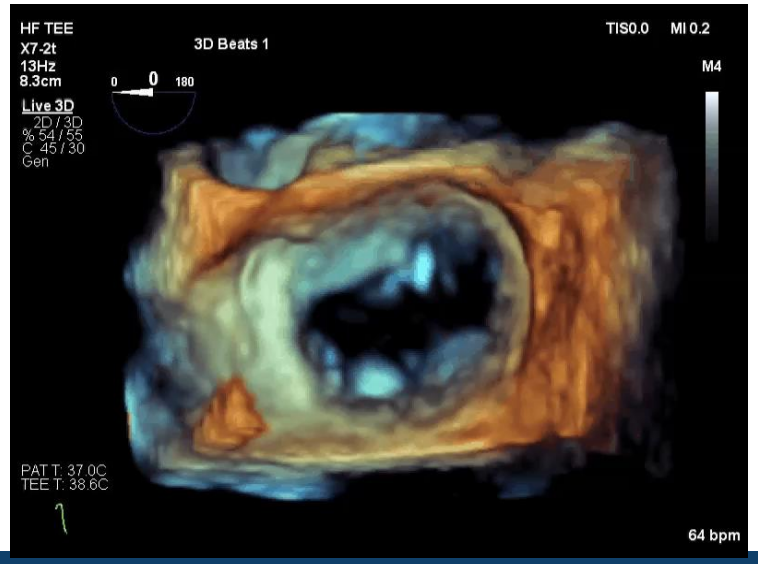
Mitra-clip
Leaflet Repair

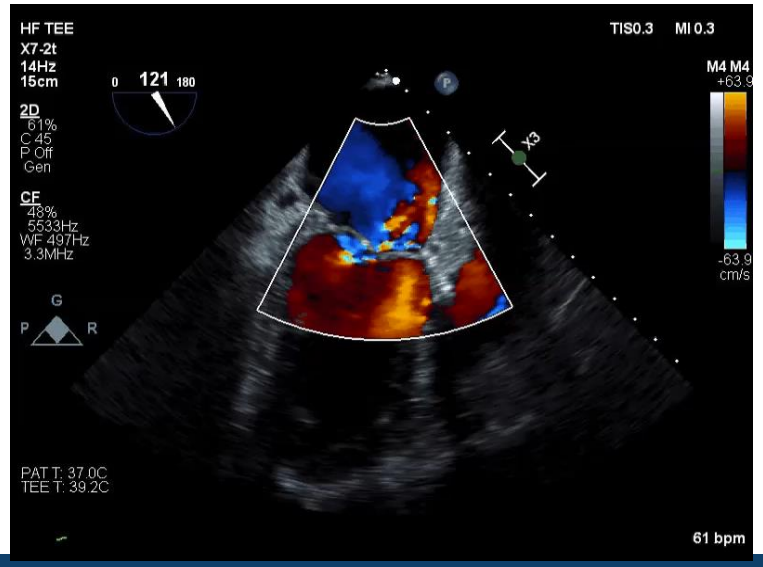


Leaflet Repair

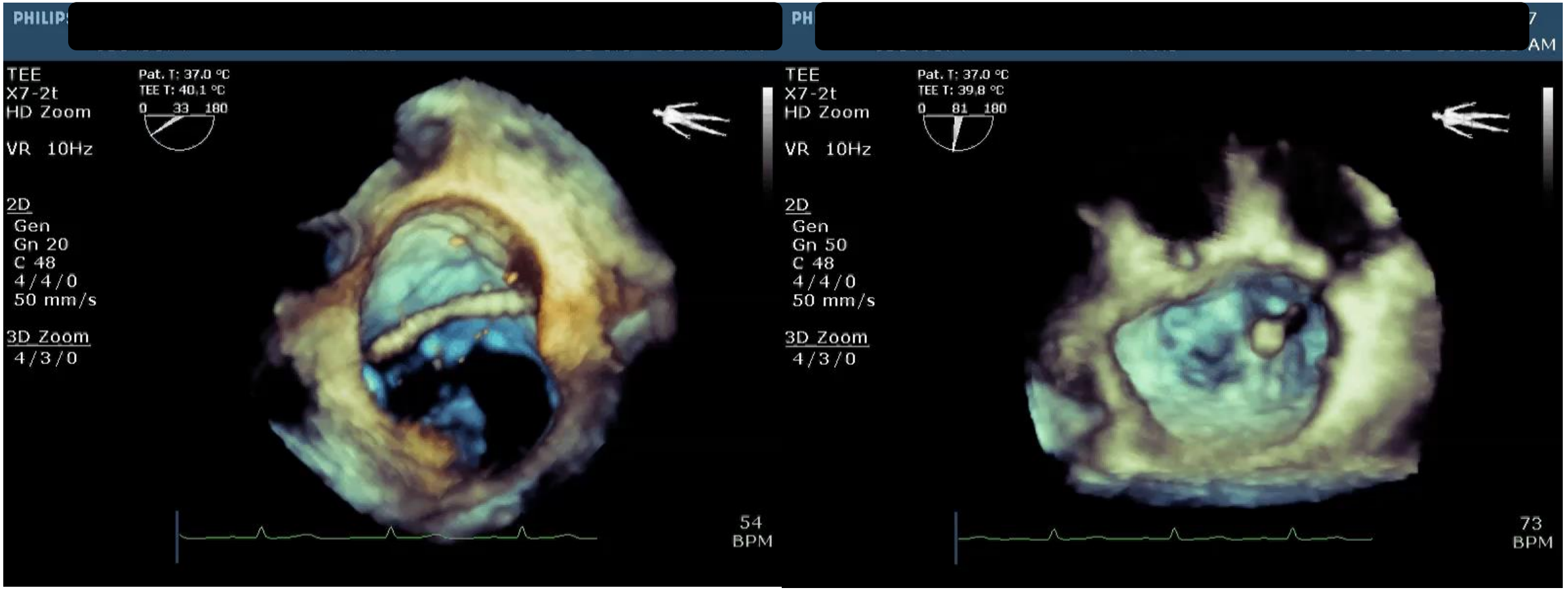




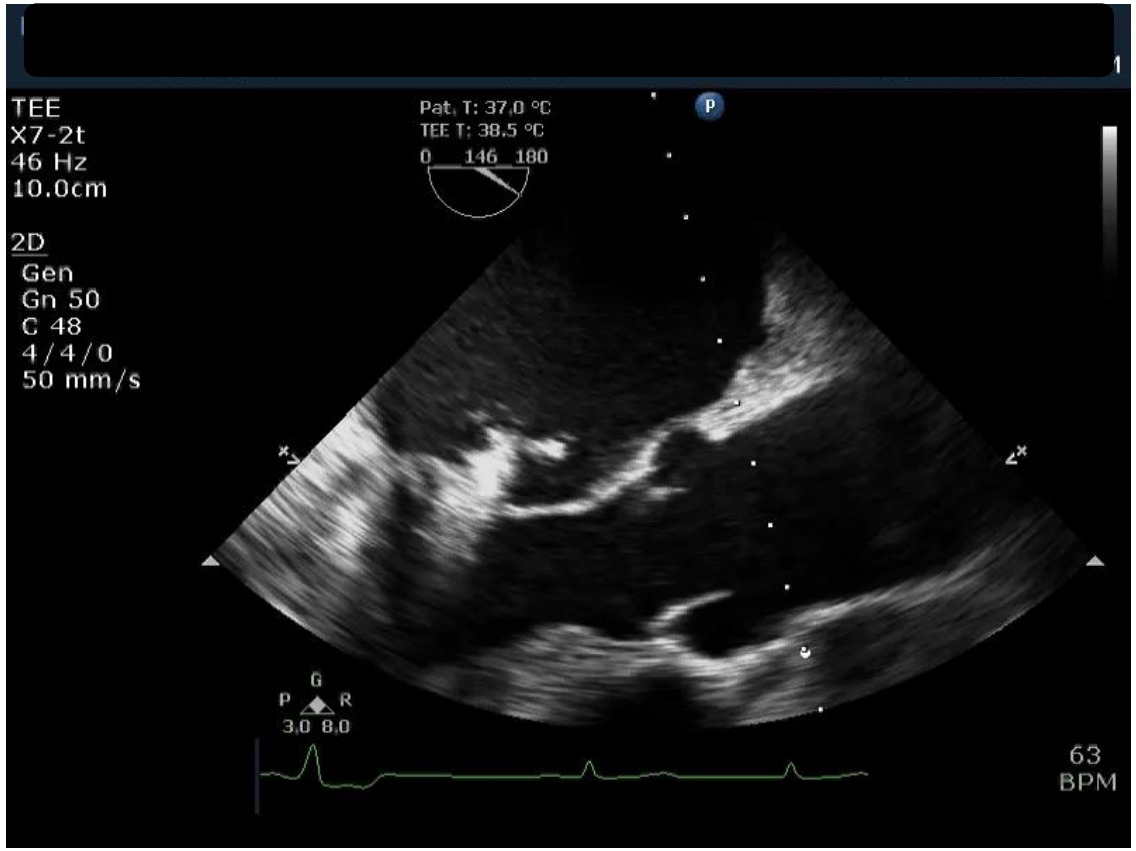


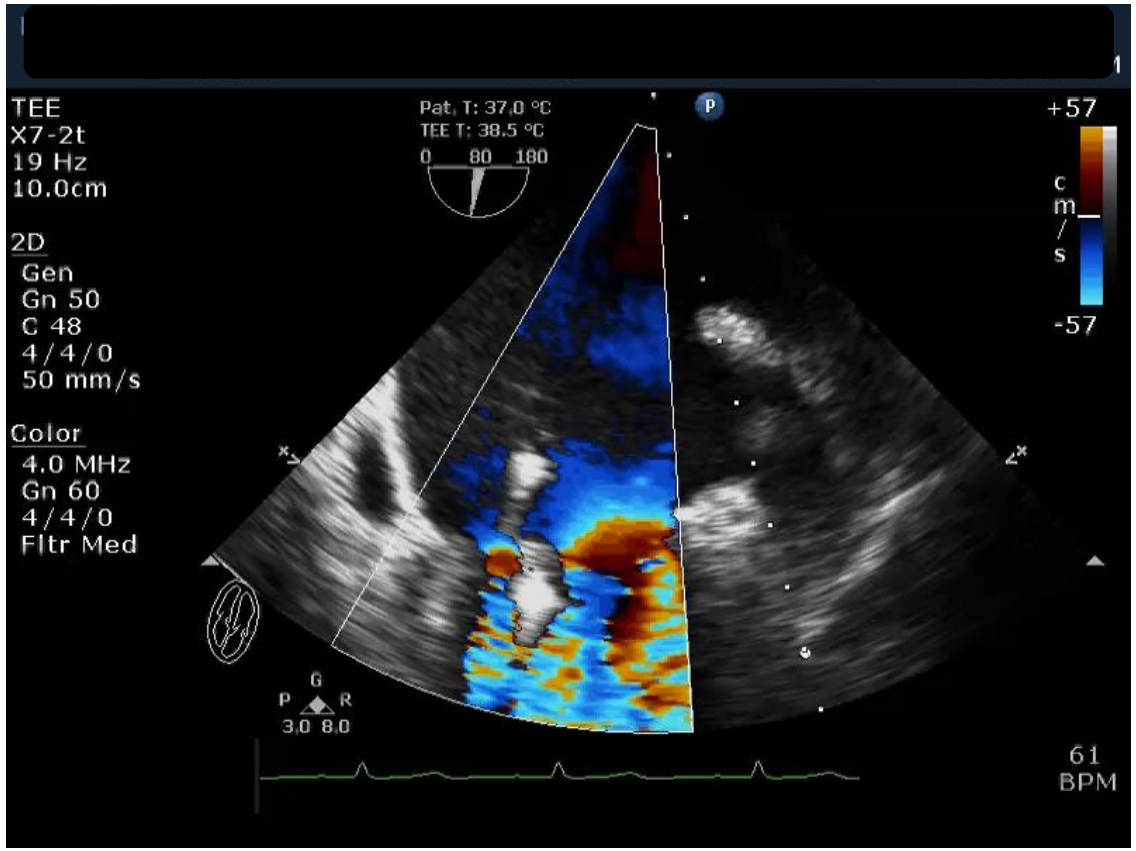


Mitra-Clip
Mitral Valve Repair



Mitra-Clip
Mitral Valve Repair





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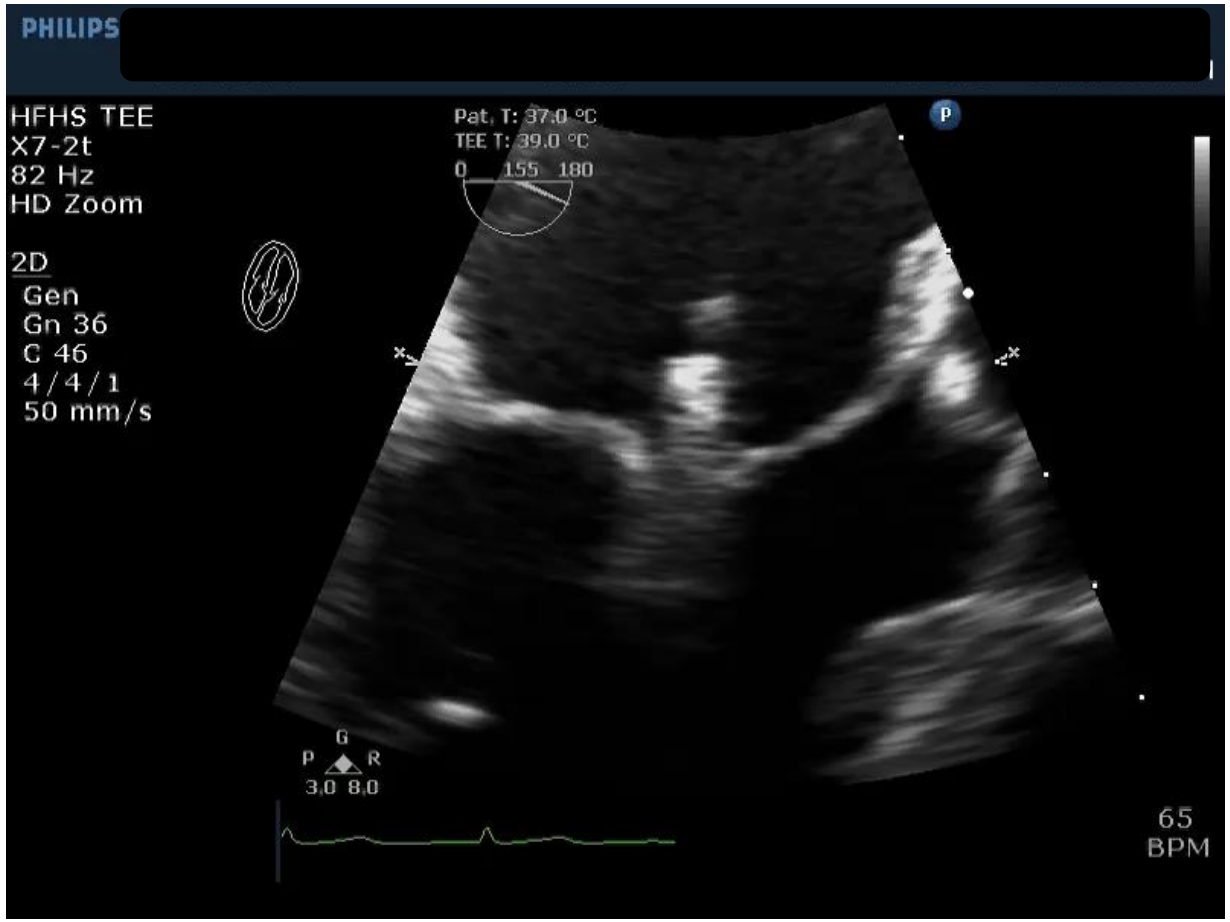
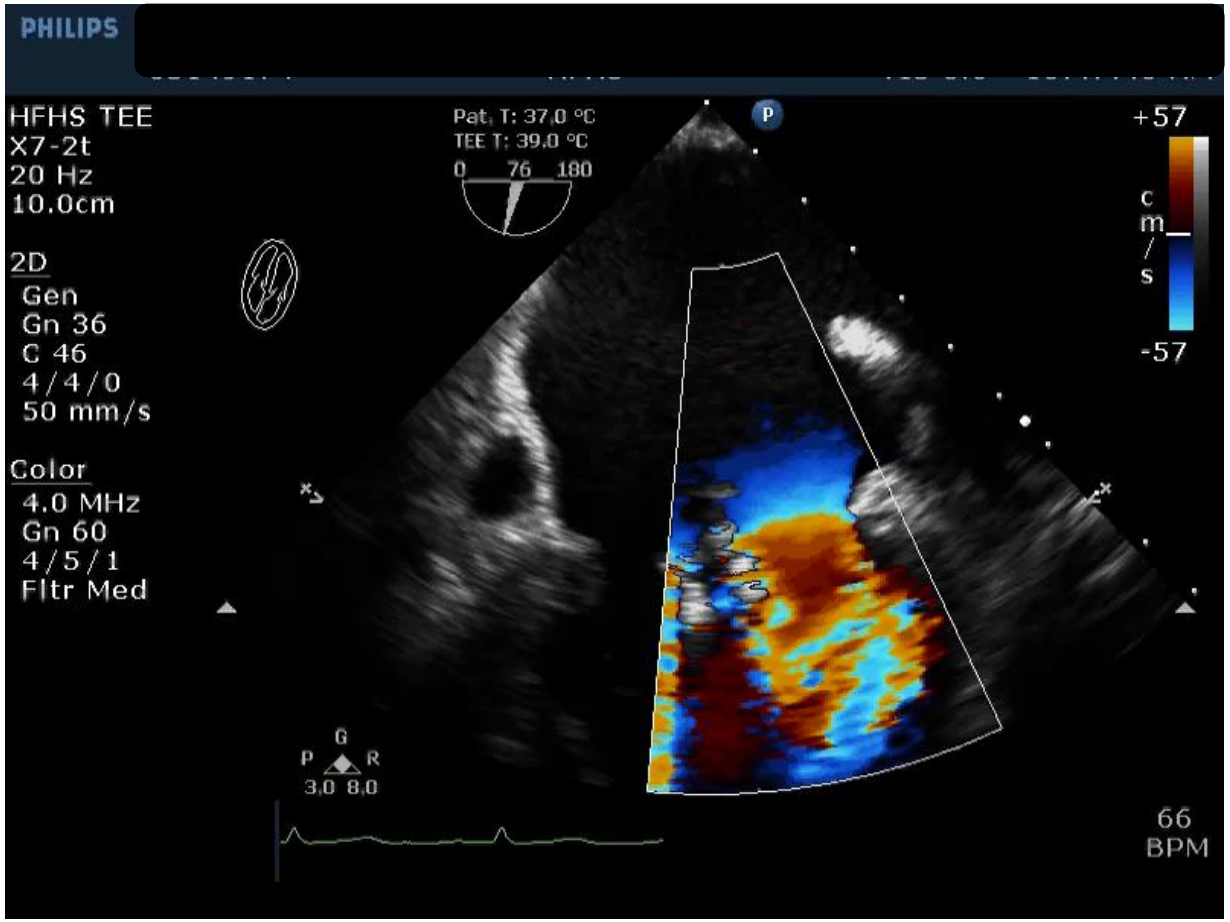
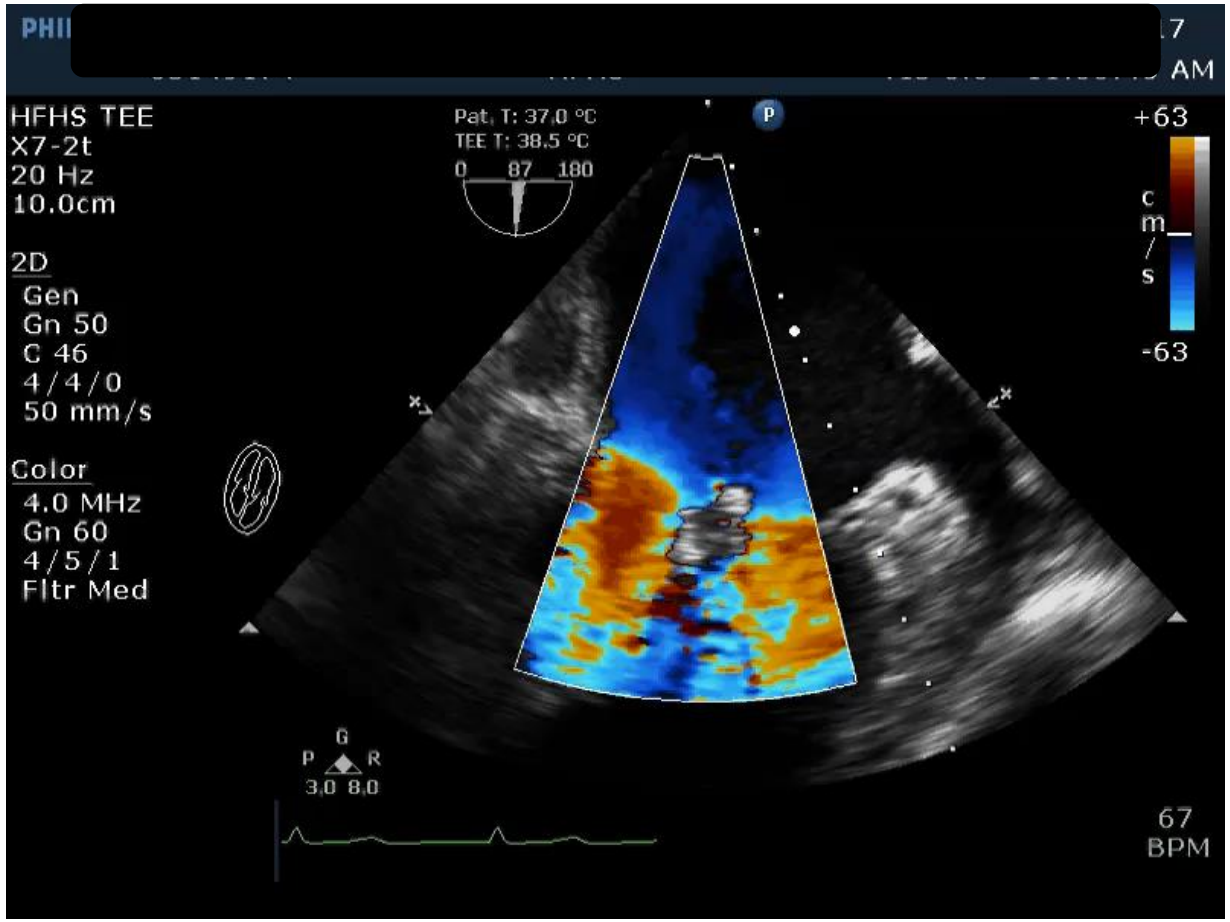
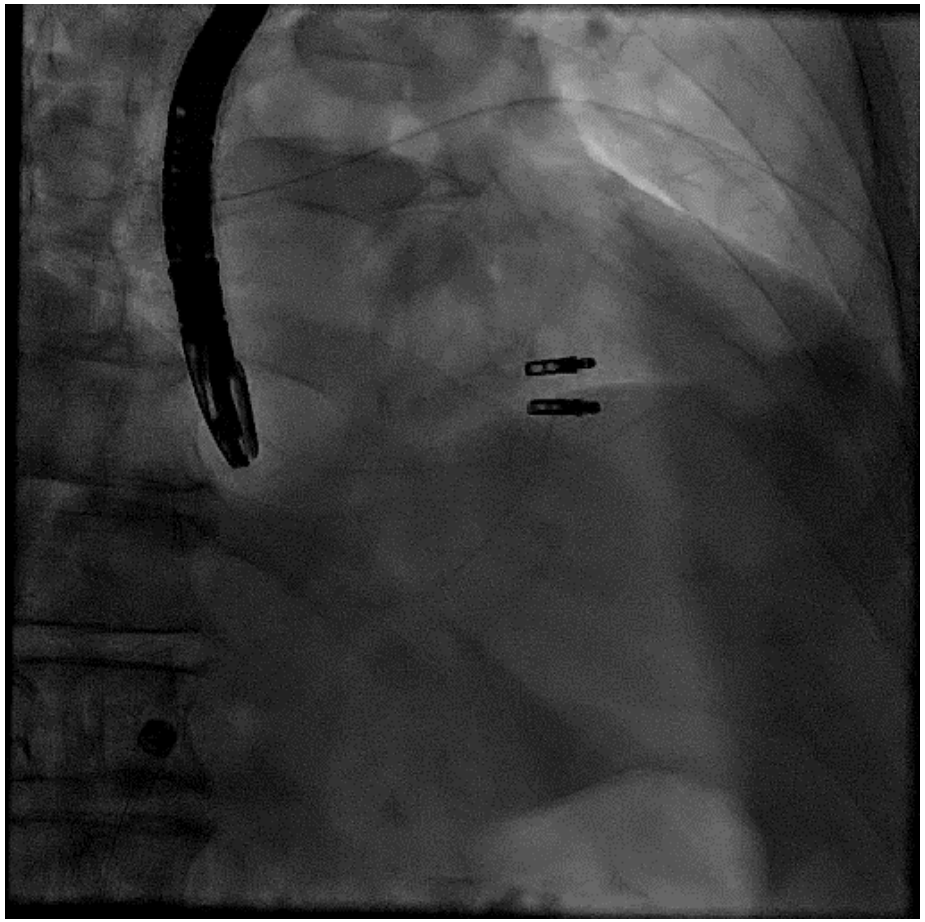




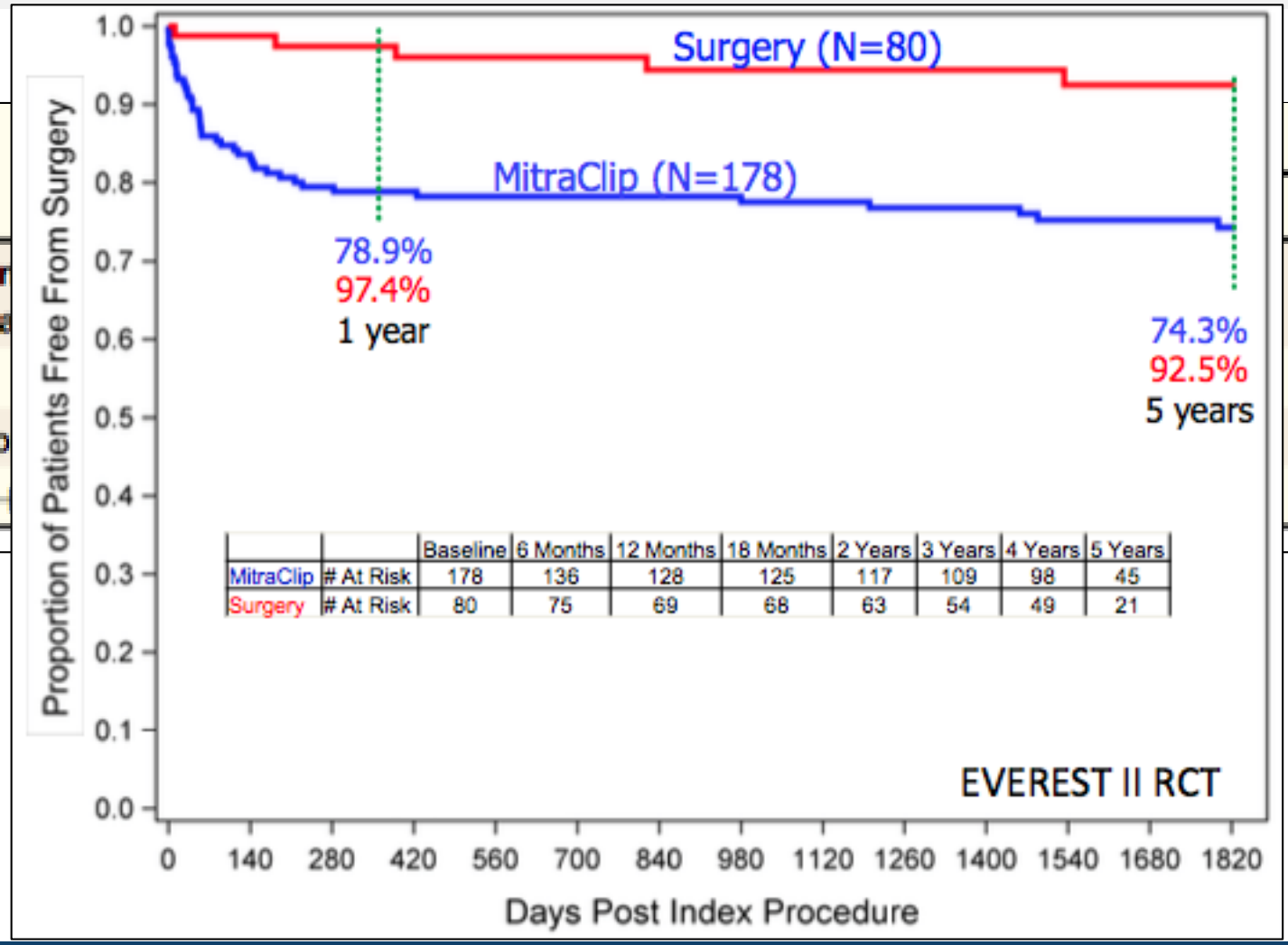
Mitra-Clip
Mitral Valve Repair





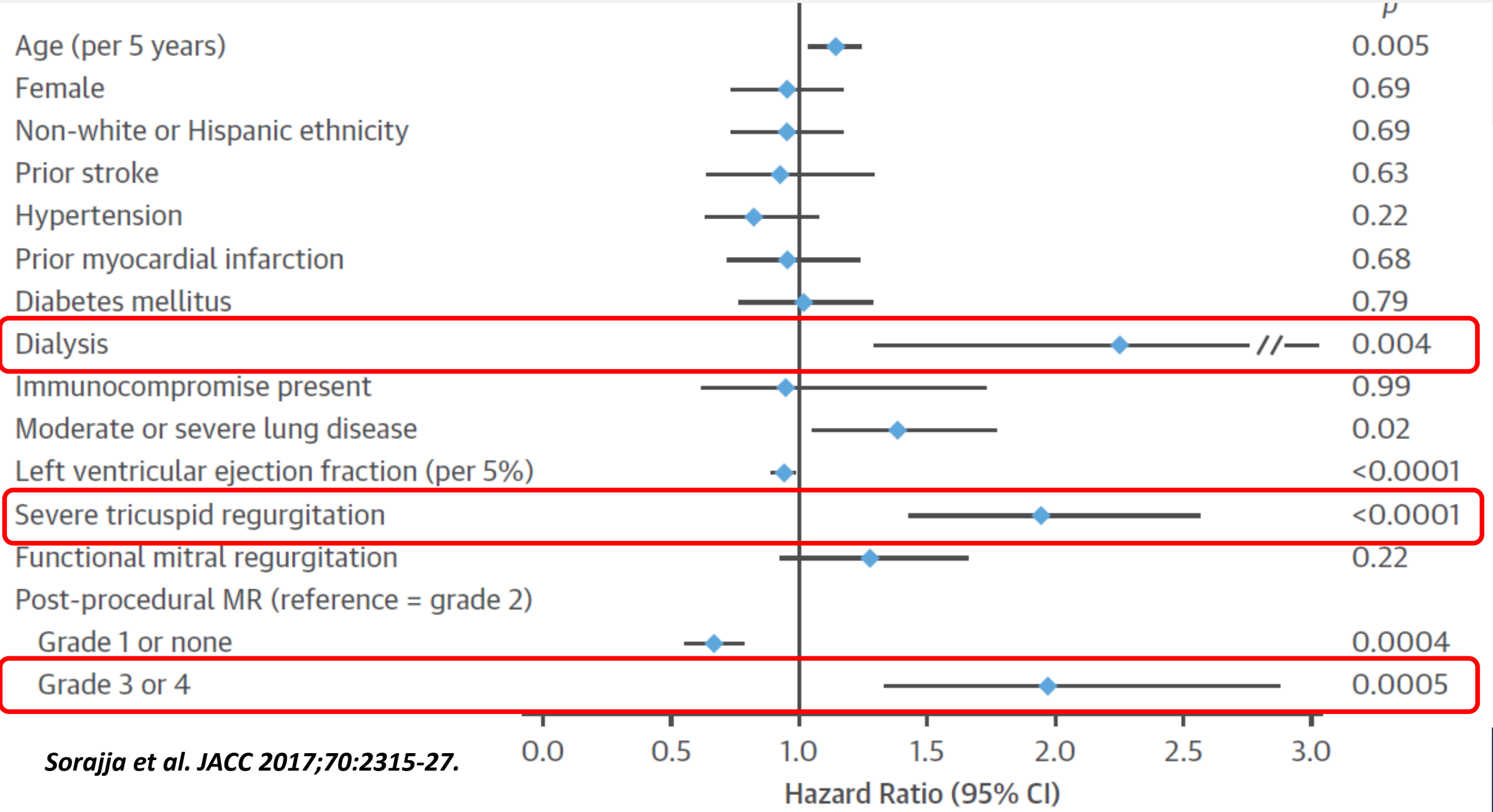
MitraClip
EVEREST II

	p Value
Freedom fror or reopera	0.070
Death	0.914
MV surgery o	<0.001
MR 3+ or 4+	0.745



		Baseline	6 Months	12 Months	18 Months	2 Years	3 Years	4 Years	5 Years
MitraClip	# At Risk	178	136	128	125	117	109	98	45
Surgery	# At Risk	80	75	69	68	63	54	49	21

Mauri L et al. JACC 2013;62:317-28.



Sorajja et al. JACC 2017;70:2315-27.

Multivariate predictors of LA pressure reduction and increased mitral gradients

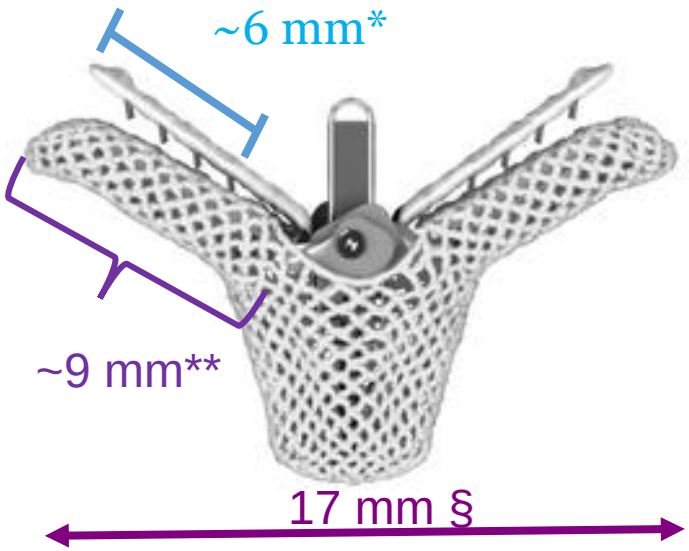
Optimal LAP Reduction		
Parameter	Adjusted Risk Ratio (95% CI)	*P* Value
Flail scallop	3.49 (1.40–9.15)	0.007
Single jet or multiple jets originating from a single scallop	3.56 (1.24–11.98)	0.02
Good or excellent 3D image quality	4.72 (1.16–32.16)	0.03

MnG >5 mm Hg Postprocedure		
Parameter	Adjusted Risk Ratio (95% CI)	*P* Value
Preprocedural MnG*	2.34 (1.27–5.07)	0.005
MAC	12.21 (2.24–109.76)	0.003
>1 Clip deployed	7.69 (1.62–48.6)	0.009

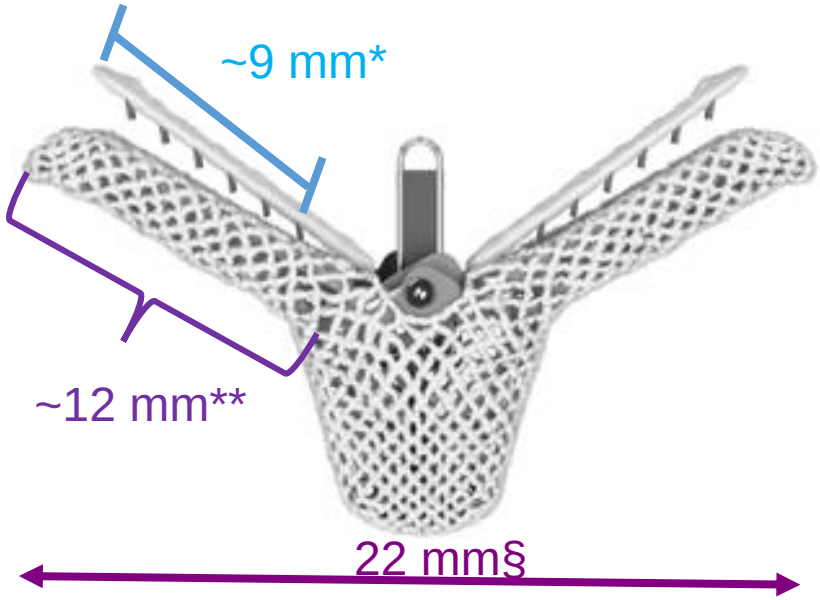
Thaden et al J Am Heart Assoc 2018;7:e007315

Mitra-Clip
New Generation

MitraClip NT / NTR

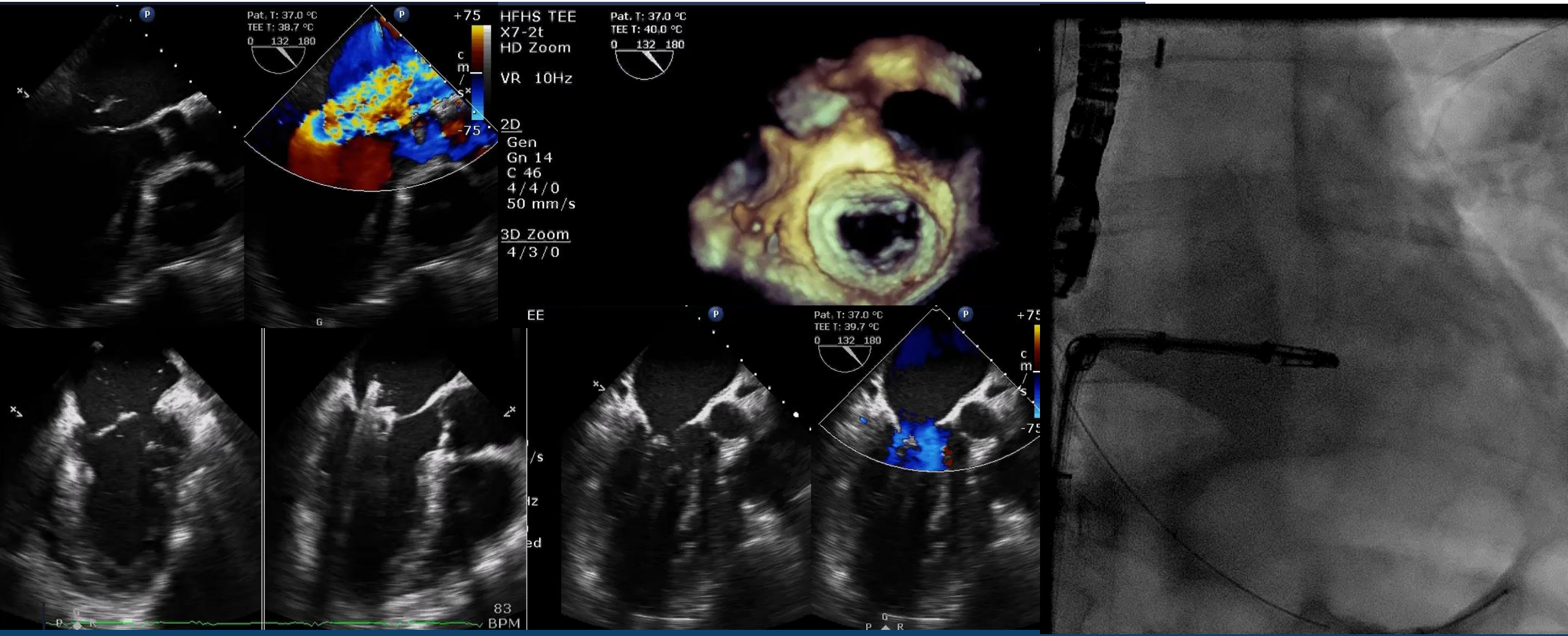


MitraClip XTR



*Leaflet insertion needed to engage all frictional elements
**Clip arm length § Clip arm span at 120 degrees

Mitra-Clip XTr
Ruptured Papillary Muscle

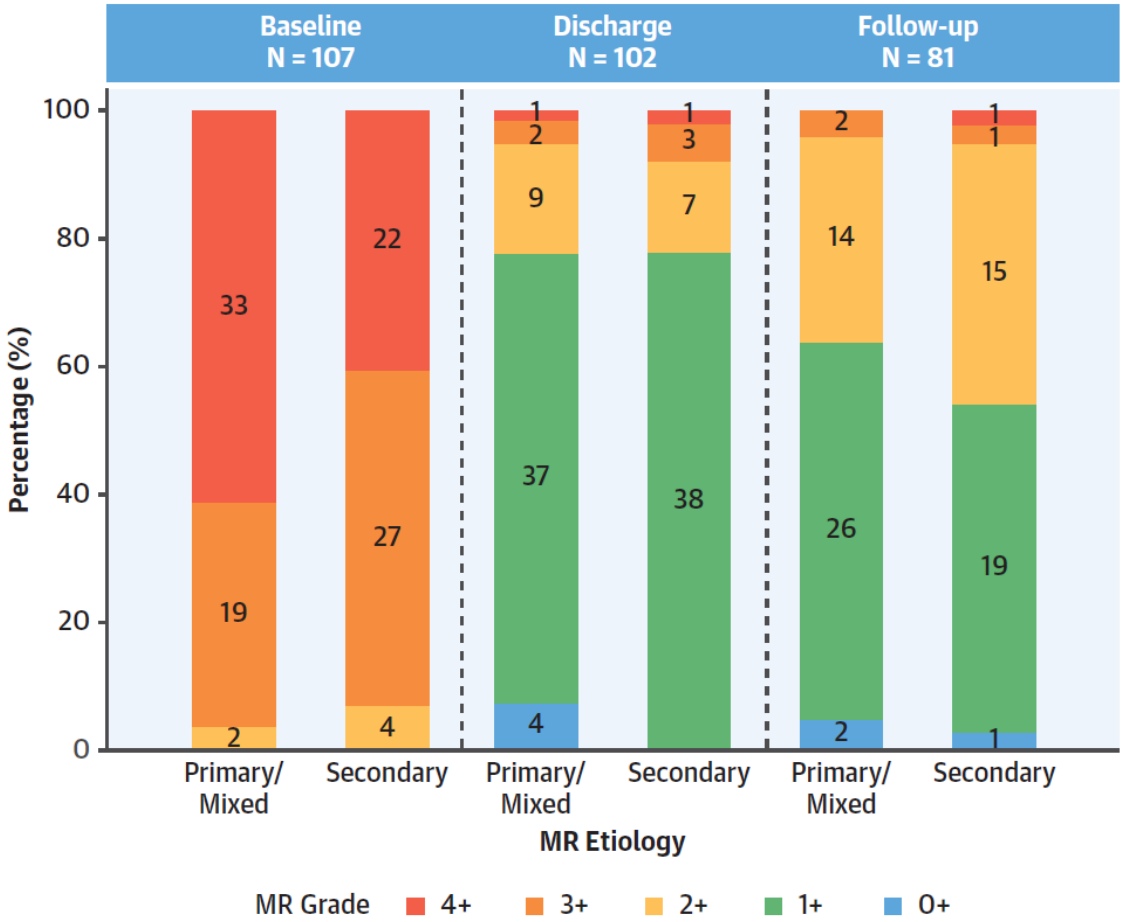


XTR Outcomes

Procedural duration, min	83 ± 45
Fluoroscopy time, min	15 ± 12
Technical success*	100 (93)
Procedural death	0
Single-leaflet device attachment	4 (4)
Isolated leaflet damage	2 (2)
Conversion to open heart surgery	4 (4)
Device embolization	0
Tamponade	0
Major access-site bleeding	3 (3)
Cerebrovascular event	0
Implantation of more than 1 device	46 (43)
Combination NTR/XTR	22 (21)
Echocardiographic result at discharge	n = 102
MR grade at discharge	
0+	4 (4)
1+	75 (73)
2+	16 (16)
3+	5 (5)
4+	2 (2)
Mean mitral valve gradient at discharge, mm Hg	3.5 ± 1.8

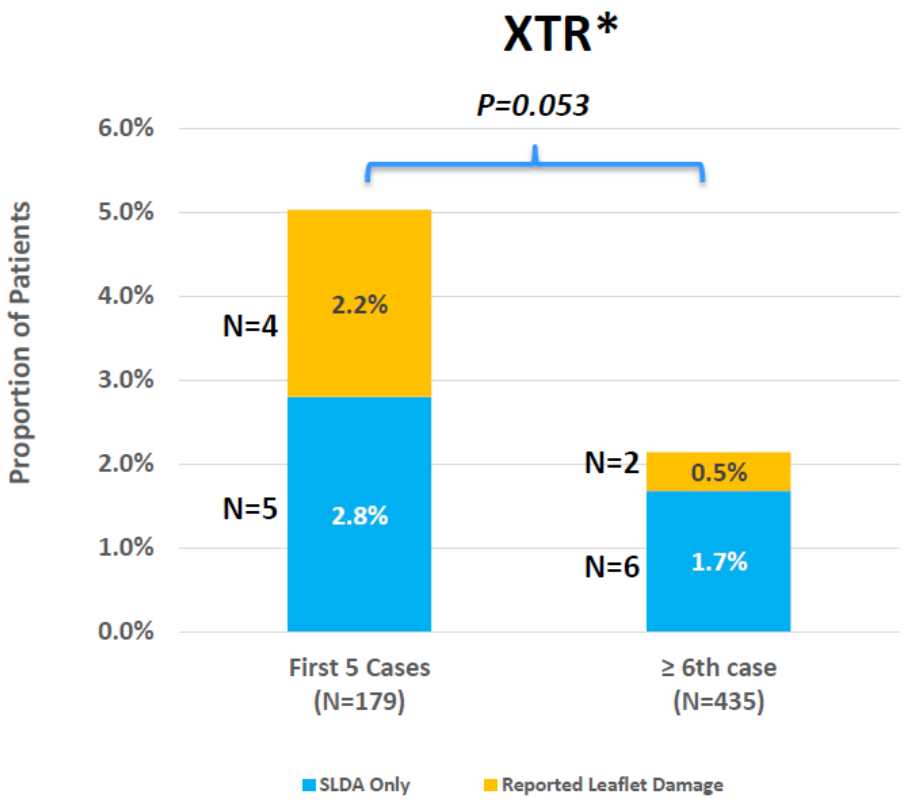
Praz F JACC Int 2019

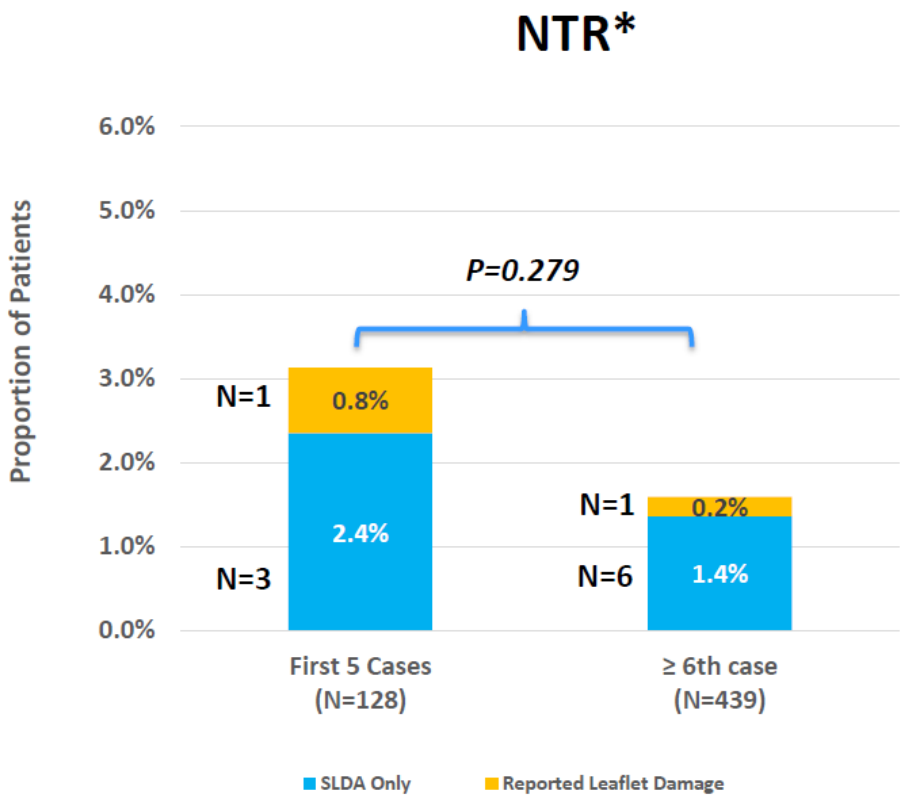
XTR
Echocardiographic outcomes



Praz, F. et al. J Am Coll Cardiol Intv. 2019;12(14):1356-65.

NTR and XTR
Early Learning Curve





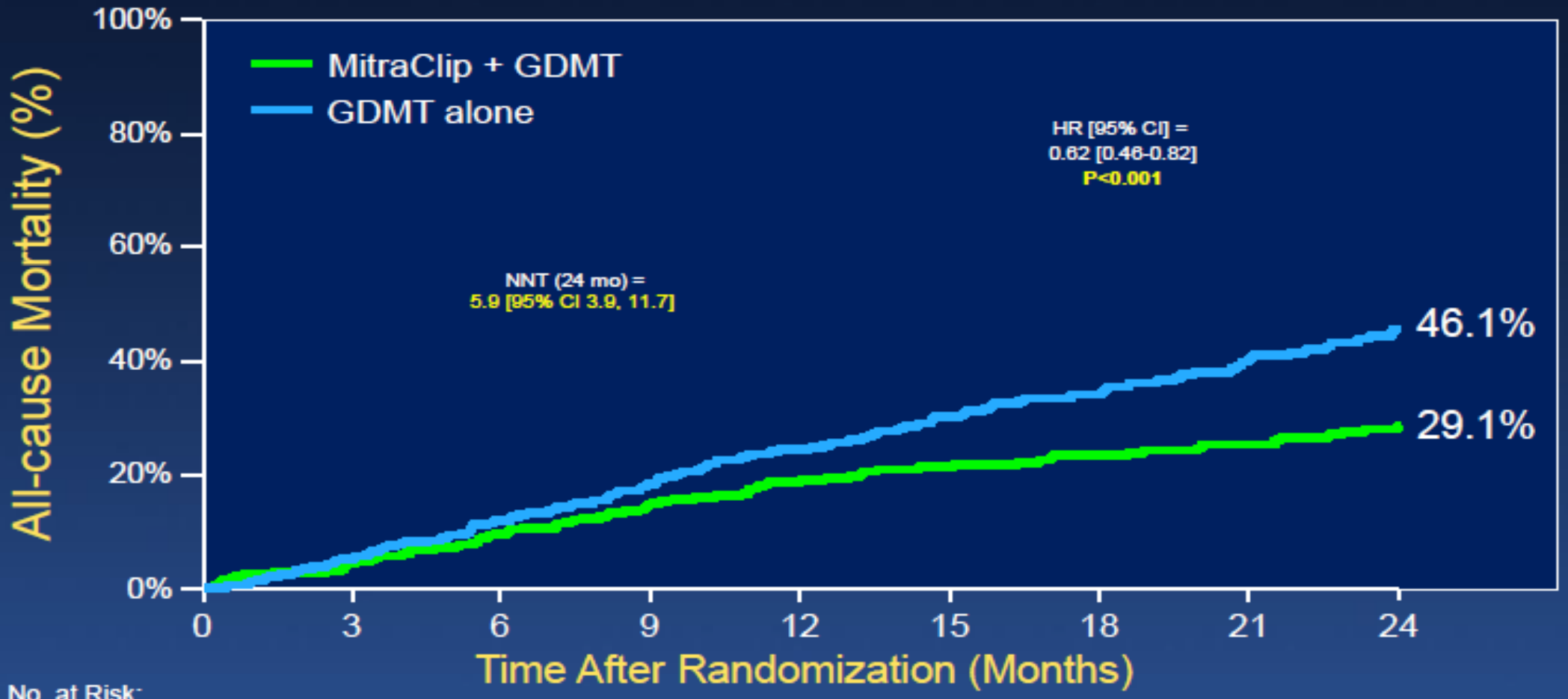
ORIGINAL ARTICLE

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*

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

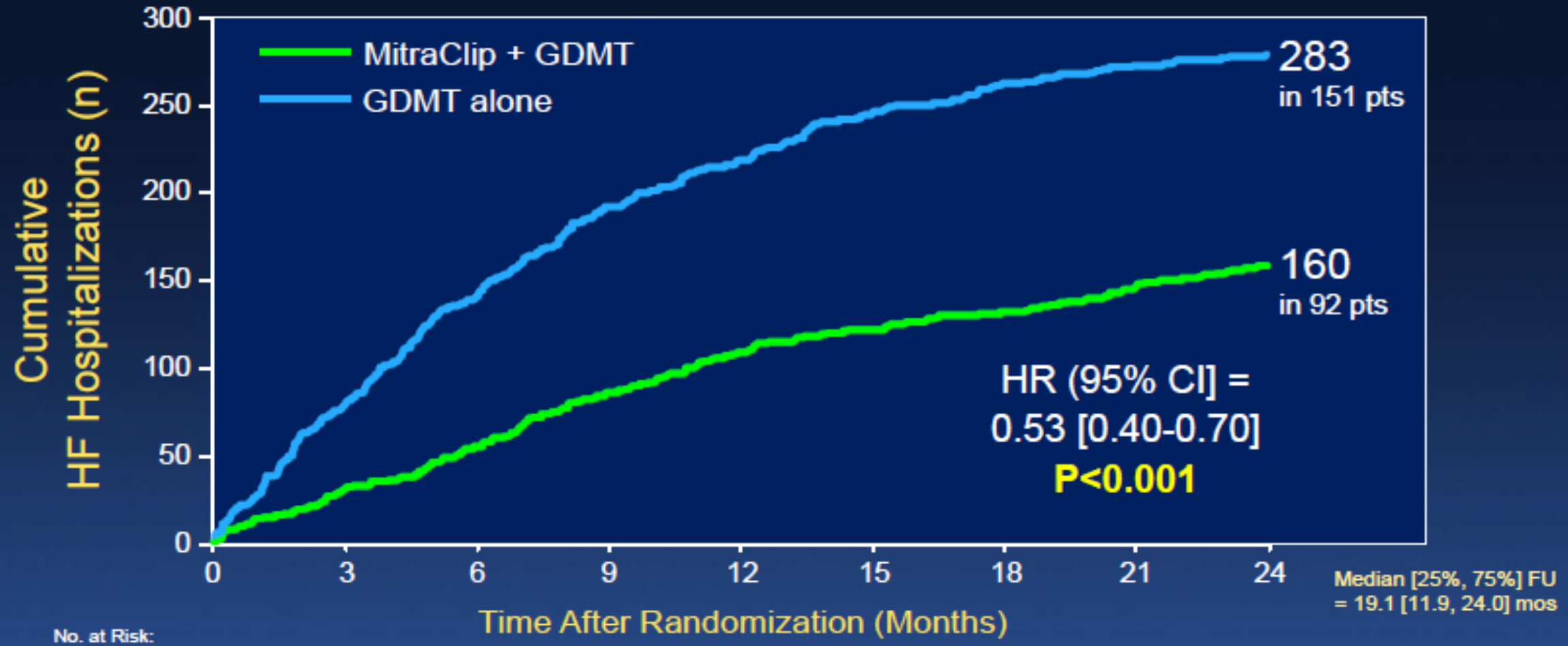
Kar S TCT 2019

COAPT TRIAL

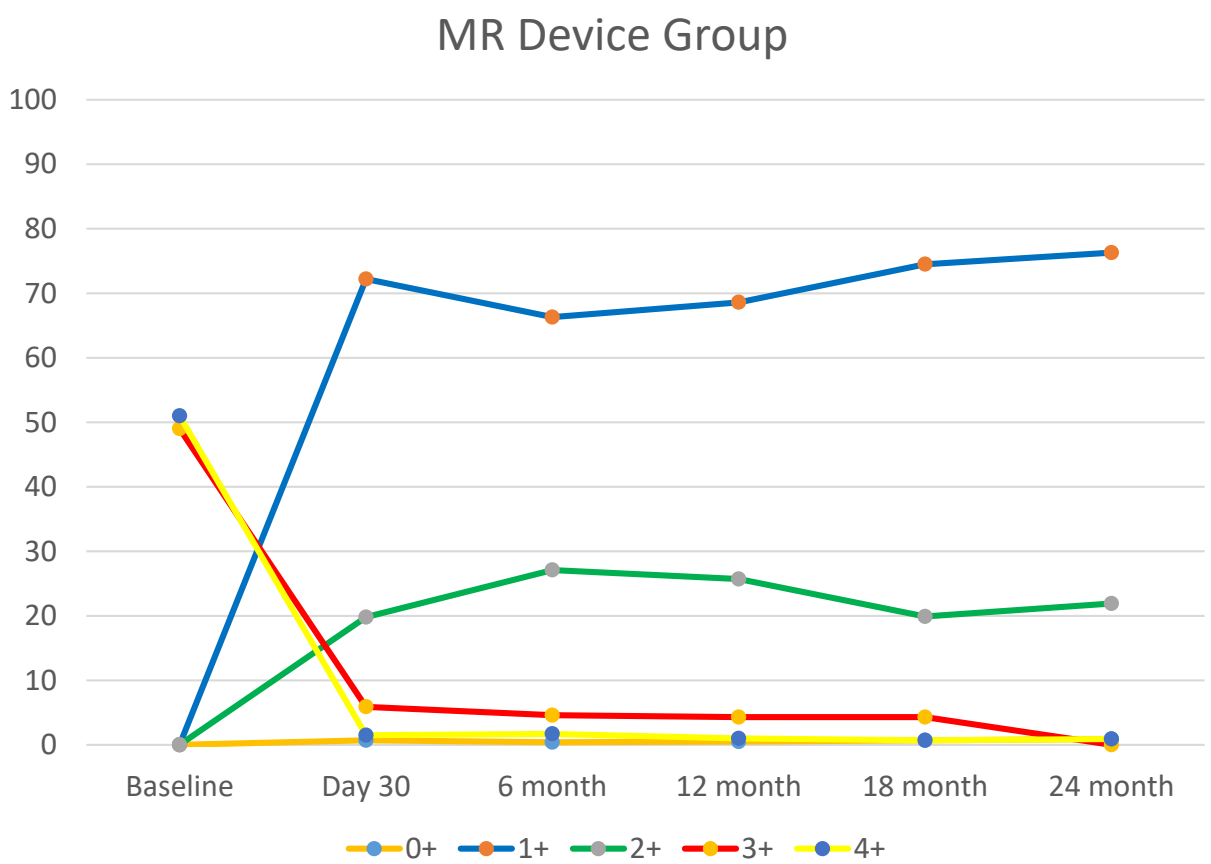
Kar S TCT 2019

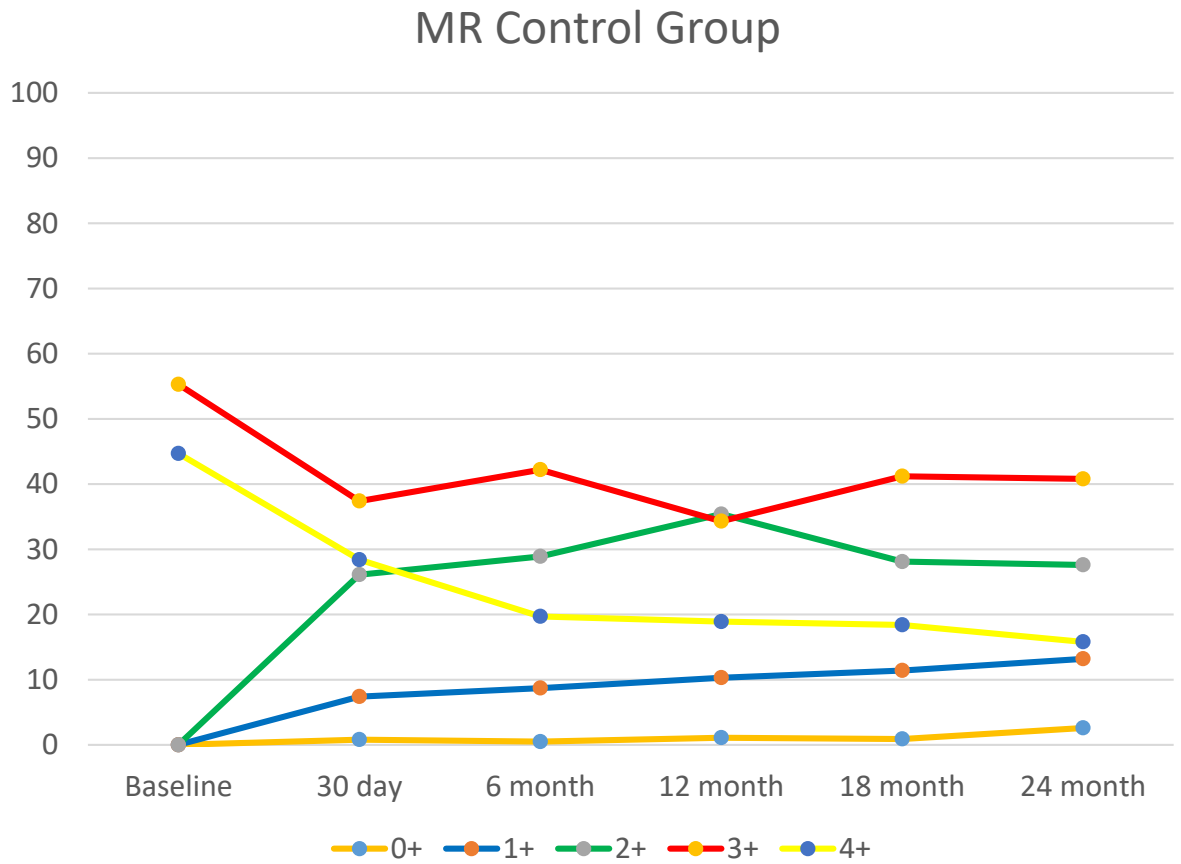
Primary Effectiveness Endpoint

All Hospitalizations for HF within 24 months



COAPT
Mitral Regurgitation over time





Stone G et al NEJM 2018

Endpoint	Device	GDMT	Hazard Ratio	P-value
1°CHF hospitalizations (2Yr)	**35.8%**	**67.9%**	**0.53 (0.4-0.7)**	<0.001
1° Freedom device complications (1yr)	**94.8%**	**---**		<0.001 Relative to goal of 0.88
Mitral Regurgitation ≤2+	**94.8%**	**46.9%**		<0.001
All cause Death (1yr)	**19.1%**	**23.2%**	**0.81 0.57-1.15)**	<0.001 for noninferiority
Death or hospitalization				
Δ KCCQ	**12.5±1.8**	**-3.6±1.9**	**16.1 (11-21.2)**	<0.001
Δ 6 min. walk distance	**-2.2±9.1**	**-60.2±9**	**57.9 (32.7-83.1)**	<0.001
All cause hospitalization	**106.2%**	**146.4%**	**0.76 (0.6-0.96)**	0.02
NYHA FC I-II	**72.2%**	**49.6%**		<0.001
Δ LVED volume	**-3.7±5.1**	**17.1±5.1**	**-20.8 (-34.9- -6.6)**	0.004
All cause death (2yr)	**29.1%**	**46.1%**	**0.62 (0.46-0.82)**	<0.001
Freedom from death, stroke, MI and nonelective cardiac surgery for a device related complication @ 30 days	**94.7%**			<0.001 for comparison with goal of 80%

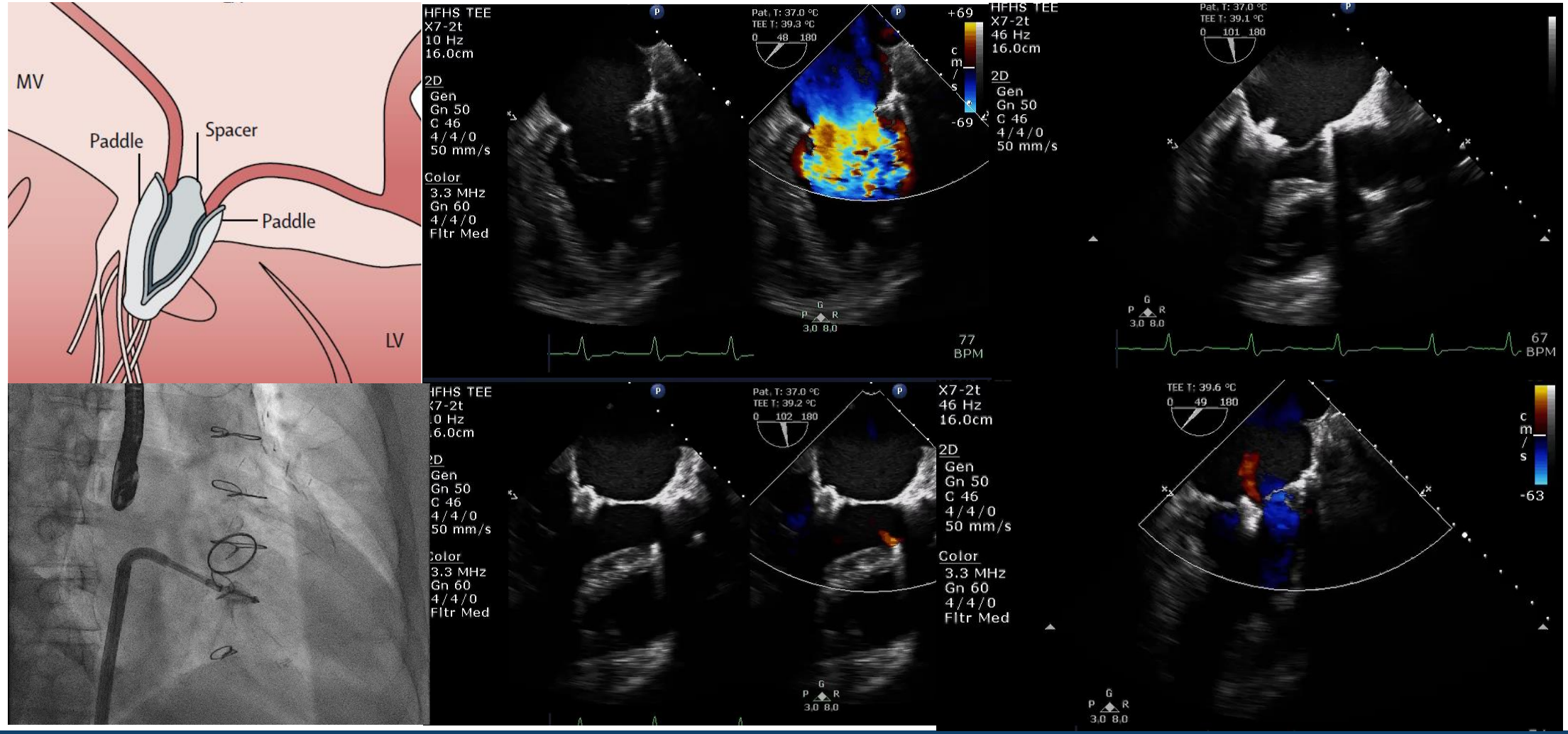
Stone G et al NEJM 2018

Mitra-Fr and COAPT Contrasts

	Mitra-Fr	COAPT
Medical Therapy	Site Determined	Central Committee
LVEF	33.3±6.5	31.3±9.1
EROA	0.31±0.1	0.41±0.5
BNP	765 (417-1281)	1014.8 ±1086
Procedural Complication rate	14.6%	3.4%
MR ≤2+ (1Yr)	~82%	94.8%
Death (1yr)	24.3%	19.1%
HF hospitalization	48.7%	35.8%

Stone G et al NEJM 2018

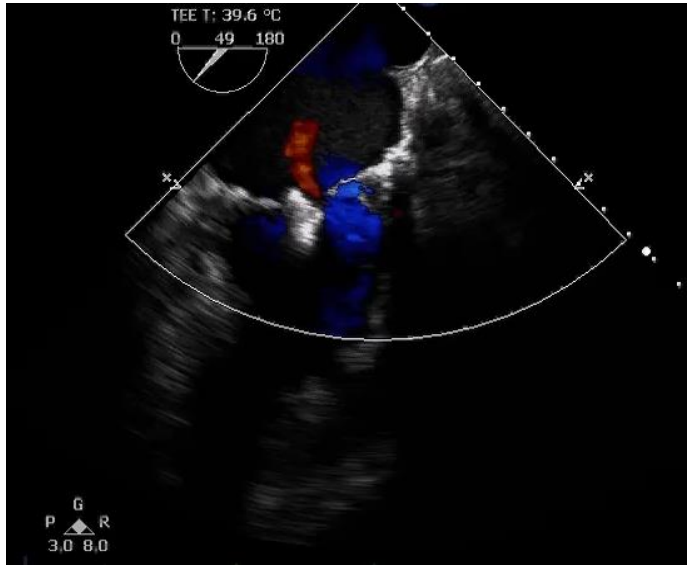
Pascal
Edge-to-edge repair



PASCAL
Early Feasibility Study

Adverse Events at 30 Days and 1 Year

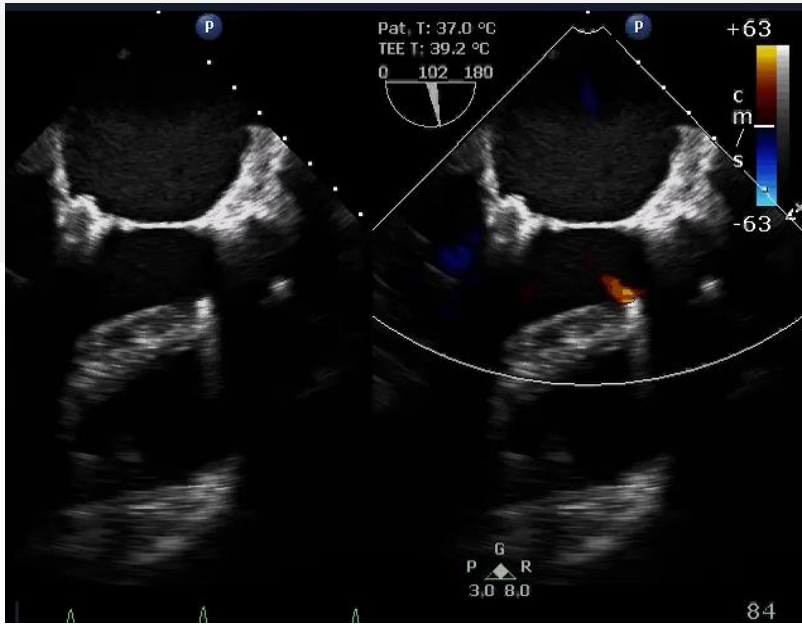
CEC Adjudicated Events	30 Days N=30 % (n)	1 Year N=30 % (n)
Cardiovascular Mortality	0.0% (0)	3.3% (1)
Stroke	0.0% (0)	0.0% (0)
Myocardial Infarction	0.0% (0)	0.0% (0)
New Need for Renal Replacement Therapy	0.0% (0)	0.0% (0)
Severe Bleeding*	6.7% (2)	16.7% (5)
Re-Intervention for Study Device-Related Complication	3.3% (1)	3.3% (1)
Composite MAE Rate, patients	**6.7% (2)**	**10.0% (3)**



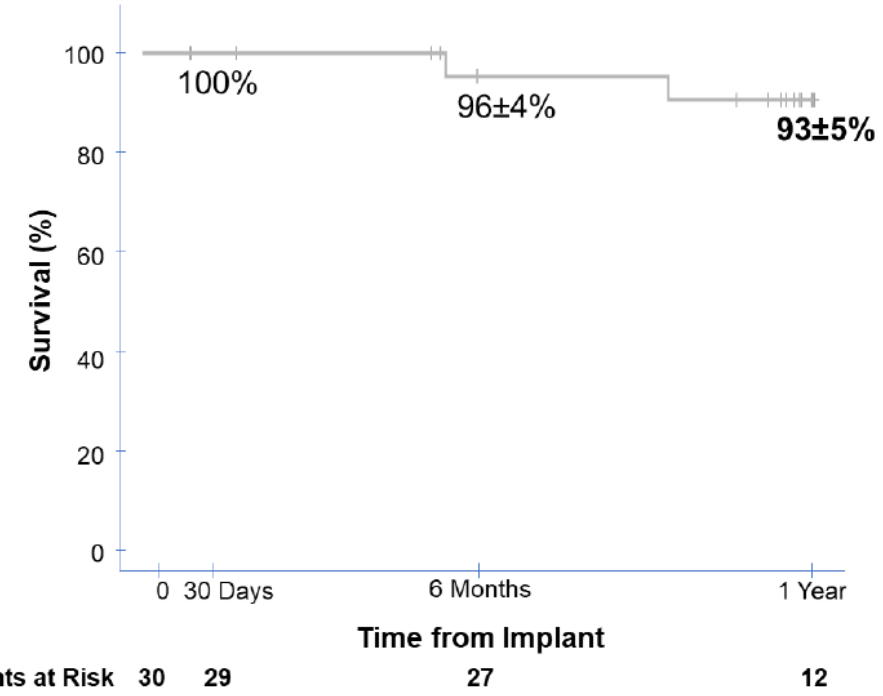
In the first 30 patient cohort, three patients experienced a total of seven events at 1 year

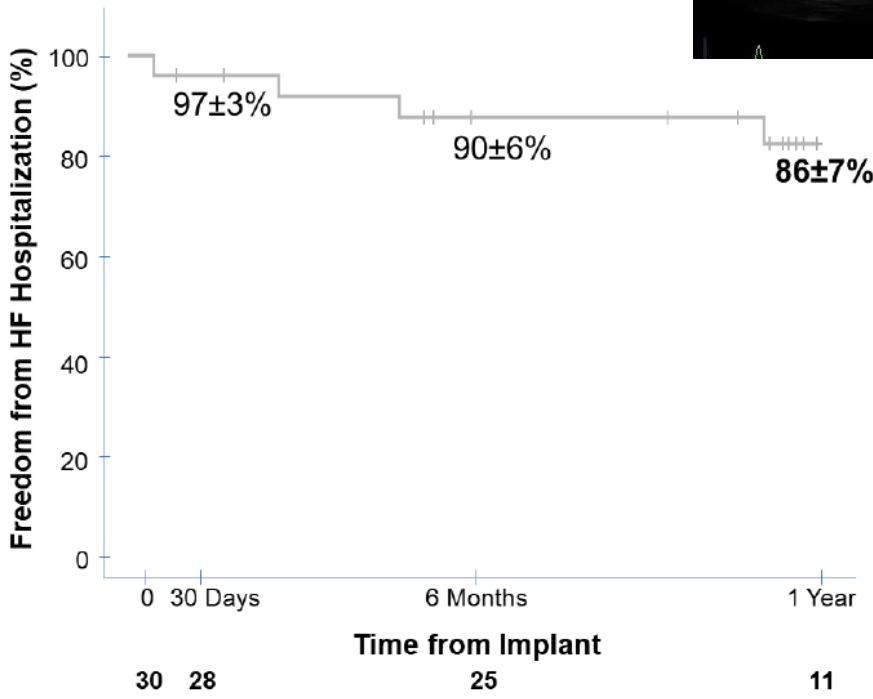
(n=1) Cardiovascular mortality due to conduction system disturbance POD 165
(n=1) Re-intervention for study device-related complication POD 00 and severe bleeding POD 01
(n=1) Procedure-related severe bleeding POD 17; recurrent GI bleeds POD 186; POD 221; POD 262

PASCAL CLASP EFS

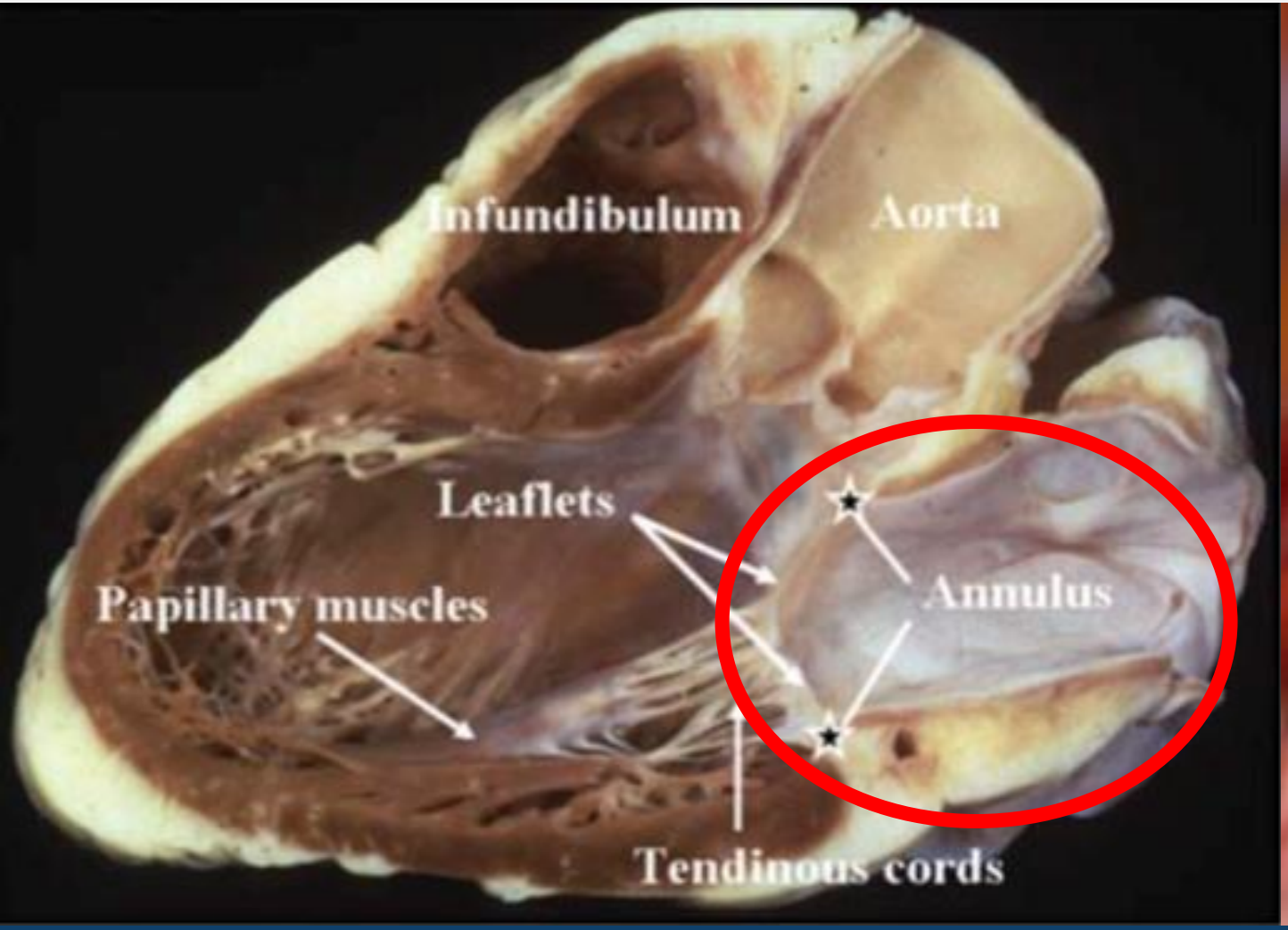


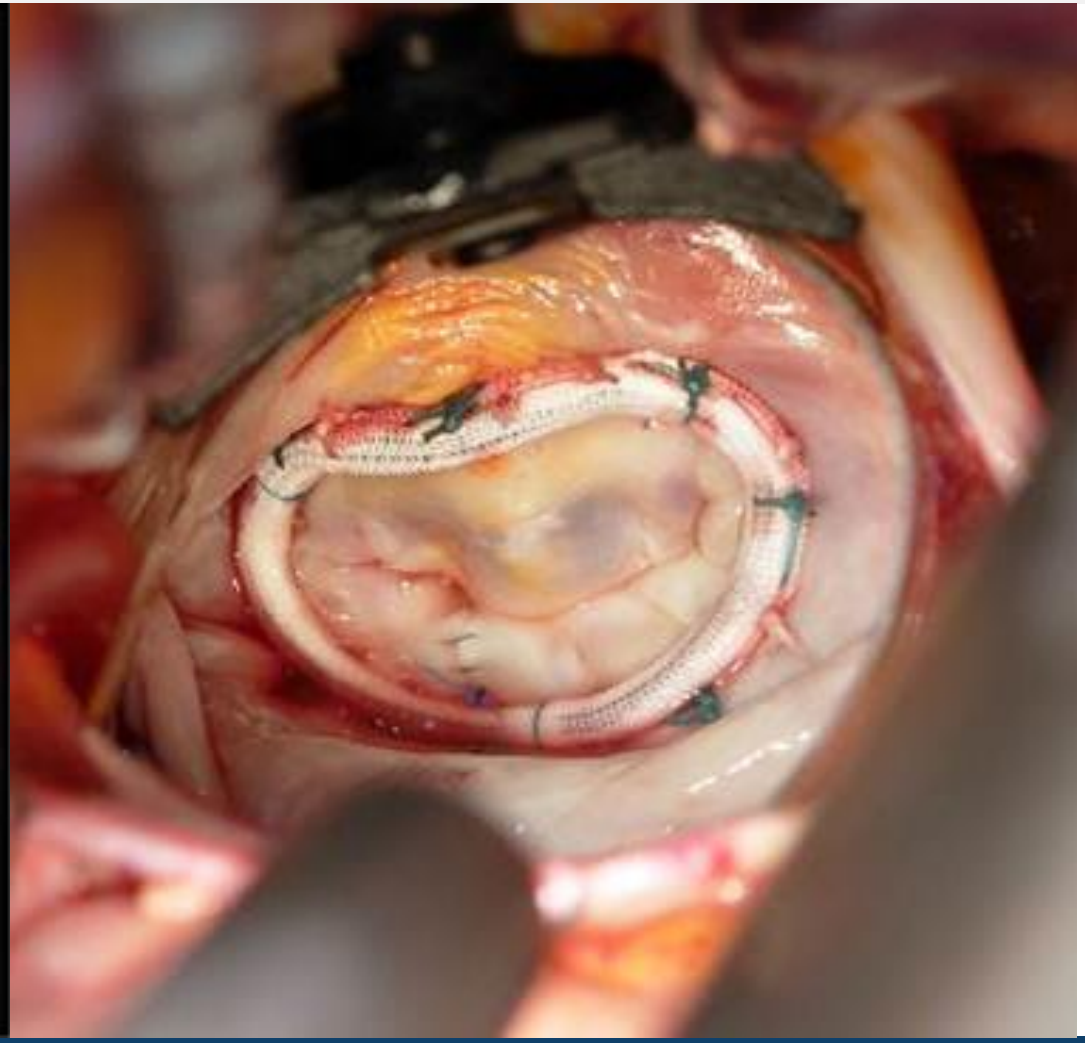
93% Survival and 86% Freedom from HF Hospitalization at 1 Year



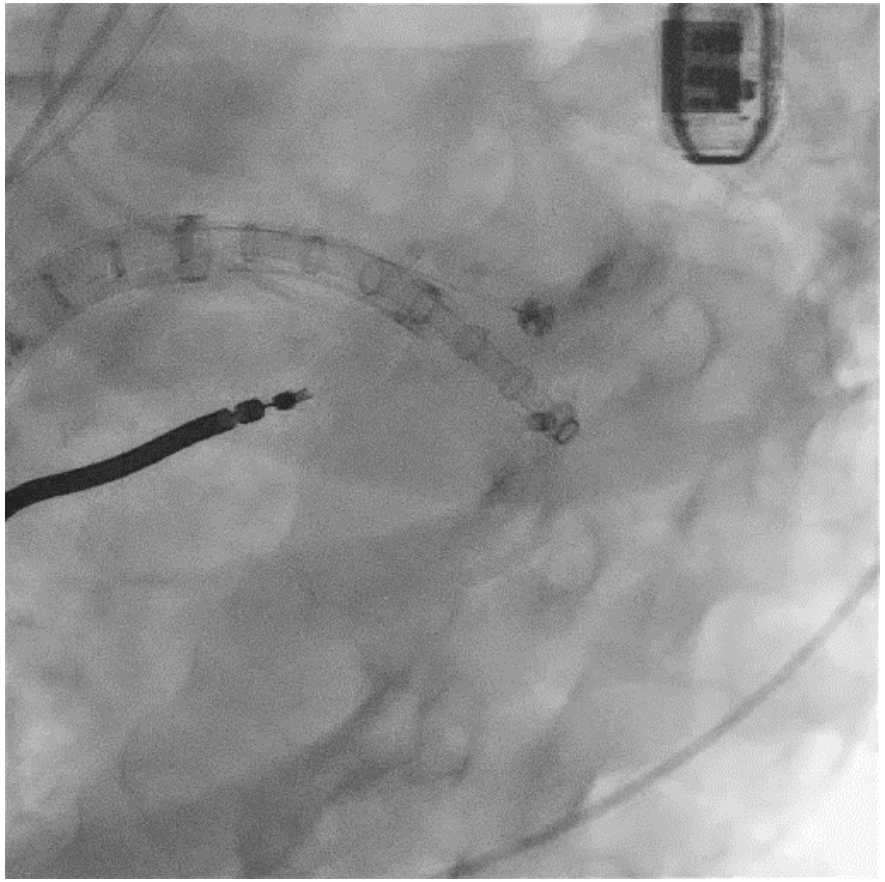


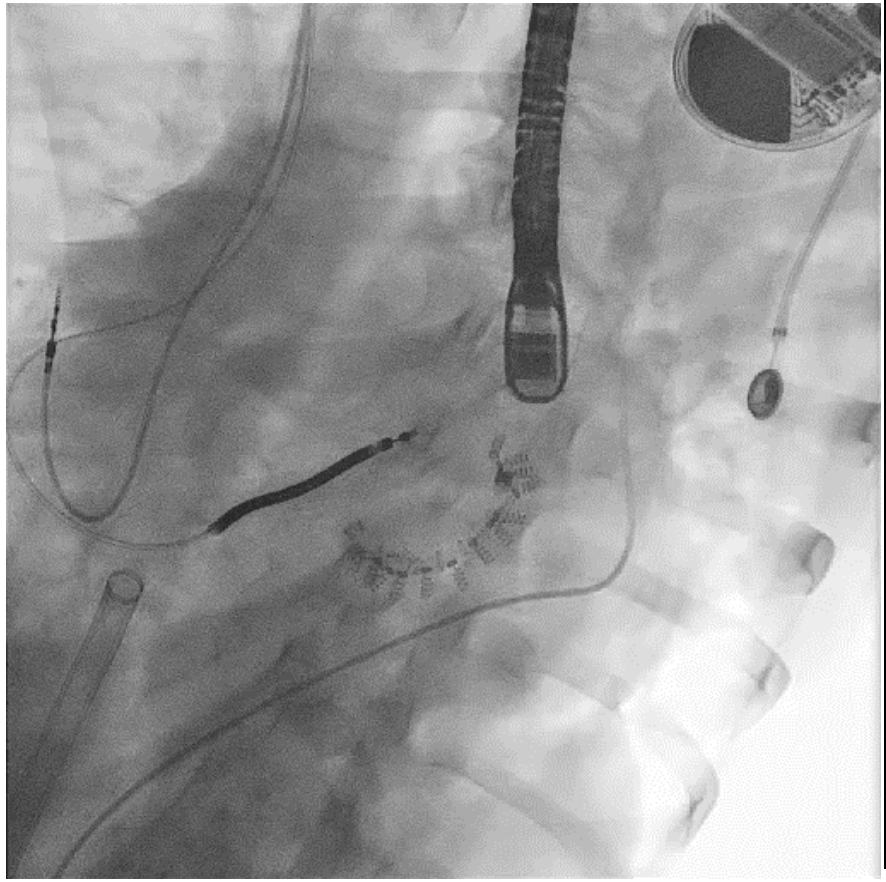
Annuloplasty technology

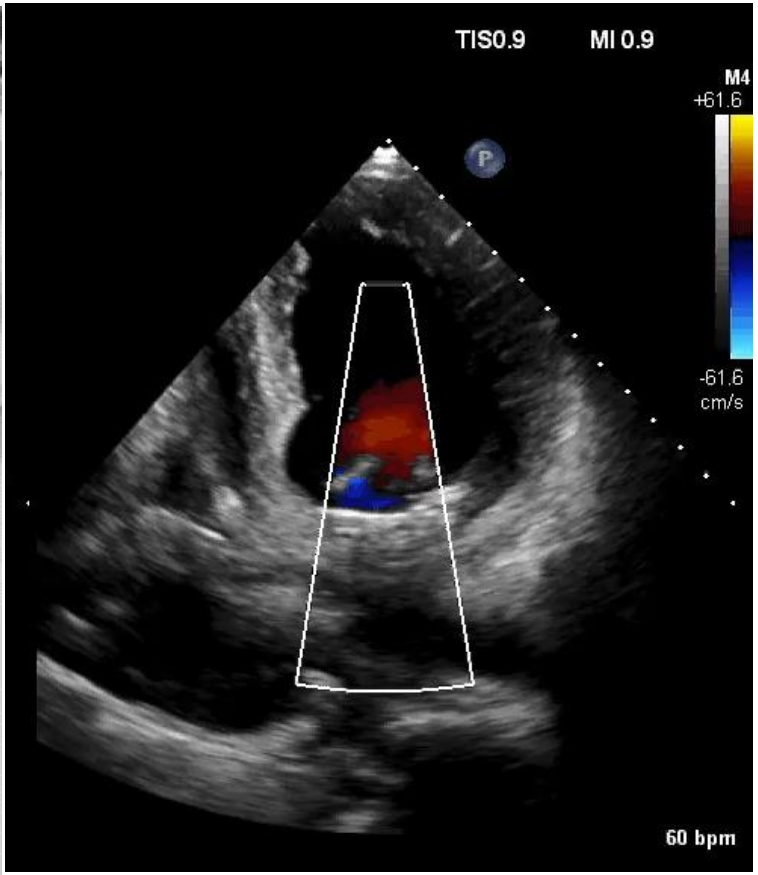




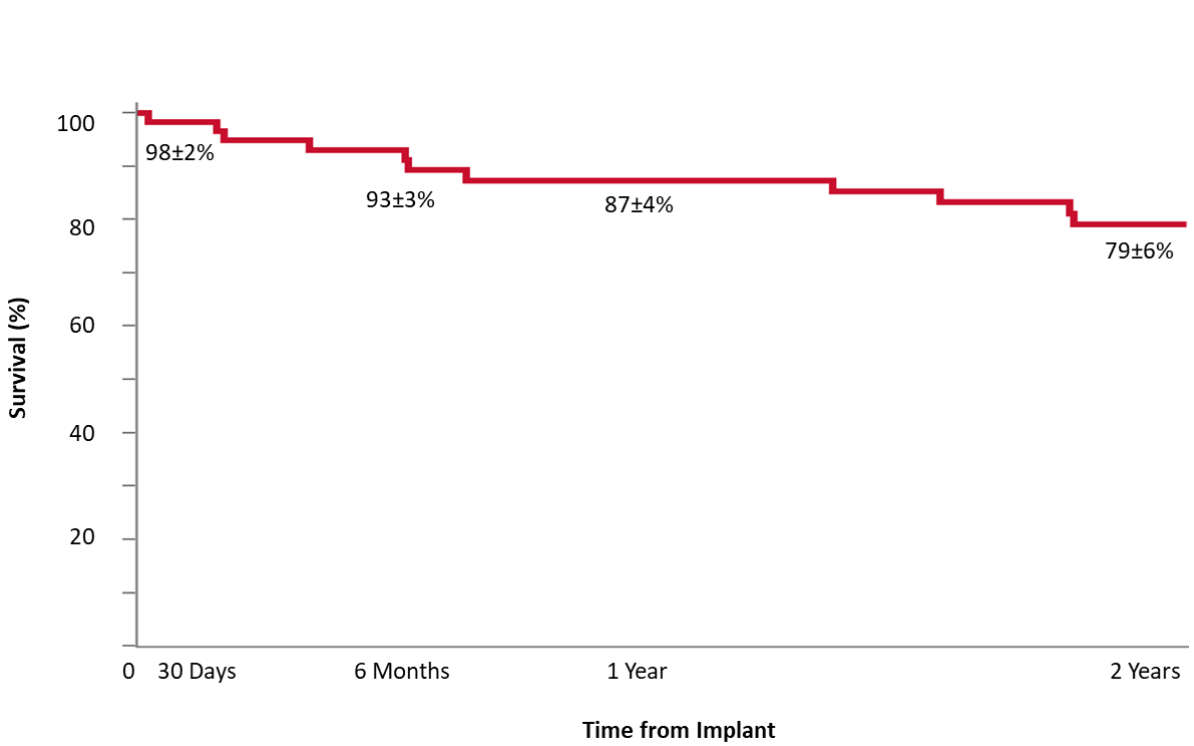
Cardioband
Mitral Annuloplasty

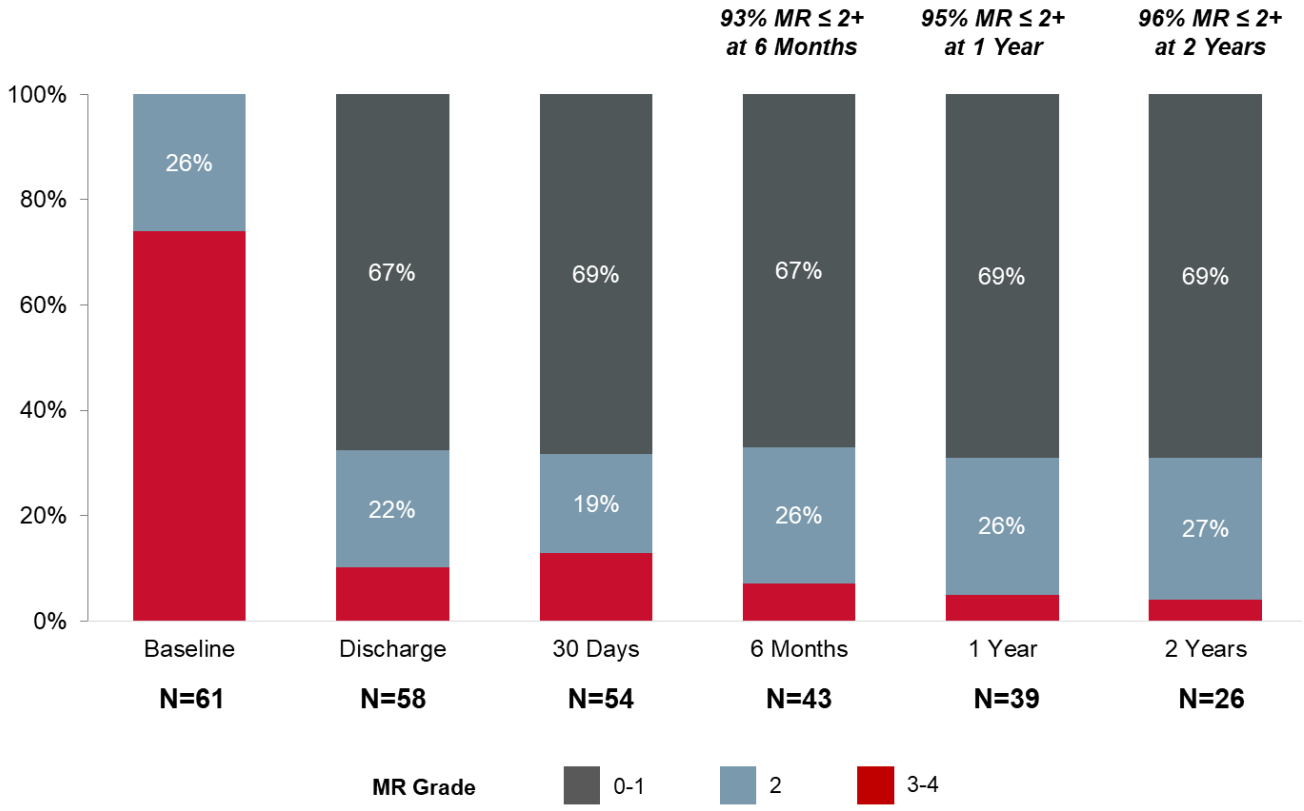






Cardioband
79% 2 year survival, sustained MR reduction @ 2 years

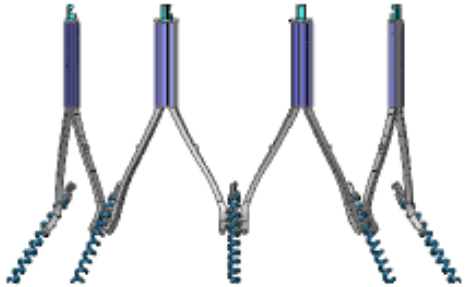




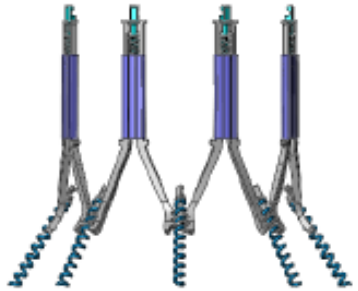
Millipede Transcatheter Repair System

- Replicates surgical repair
- TEE and ICE Navigation
- Repositionable
- Future interventions will be feasible if necessary

Placement



Anchor



Actuate

Millipede

Guide Catheter

Delivery Catheter

ICE Catheter

Familiar steering to land device

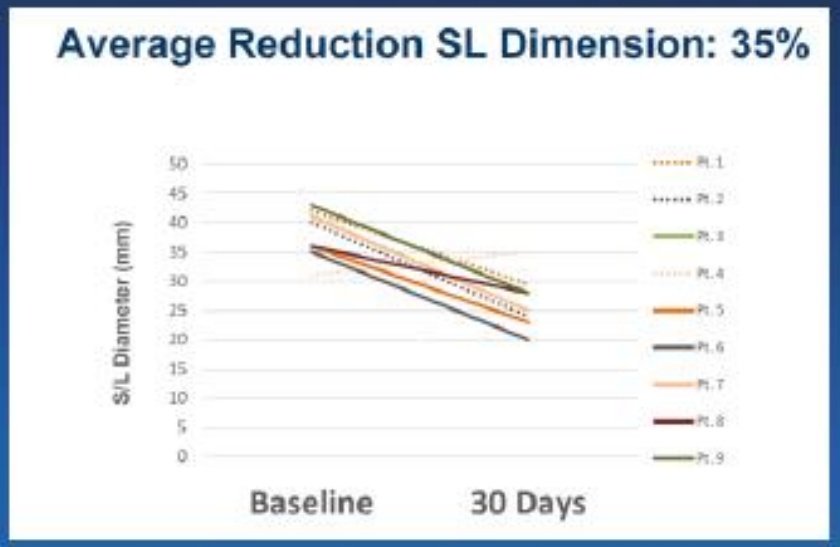
Adjustment knobs control anchoring and actuation

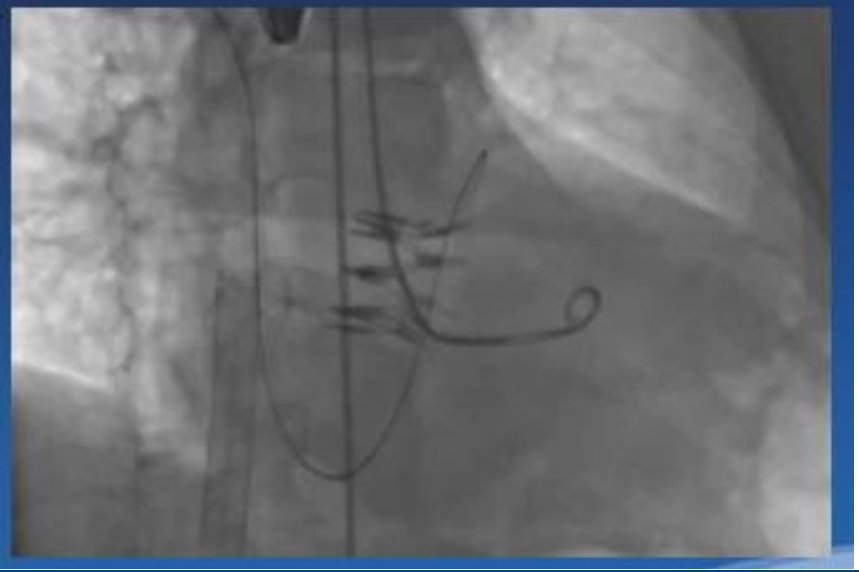
Standard imaging:
- Fluoro to access left atrium
- TEE to land device
- ICE to locate anchors

Millipede

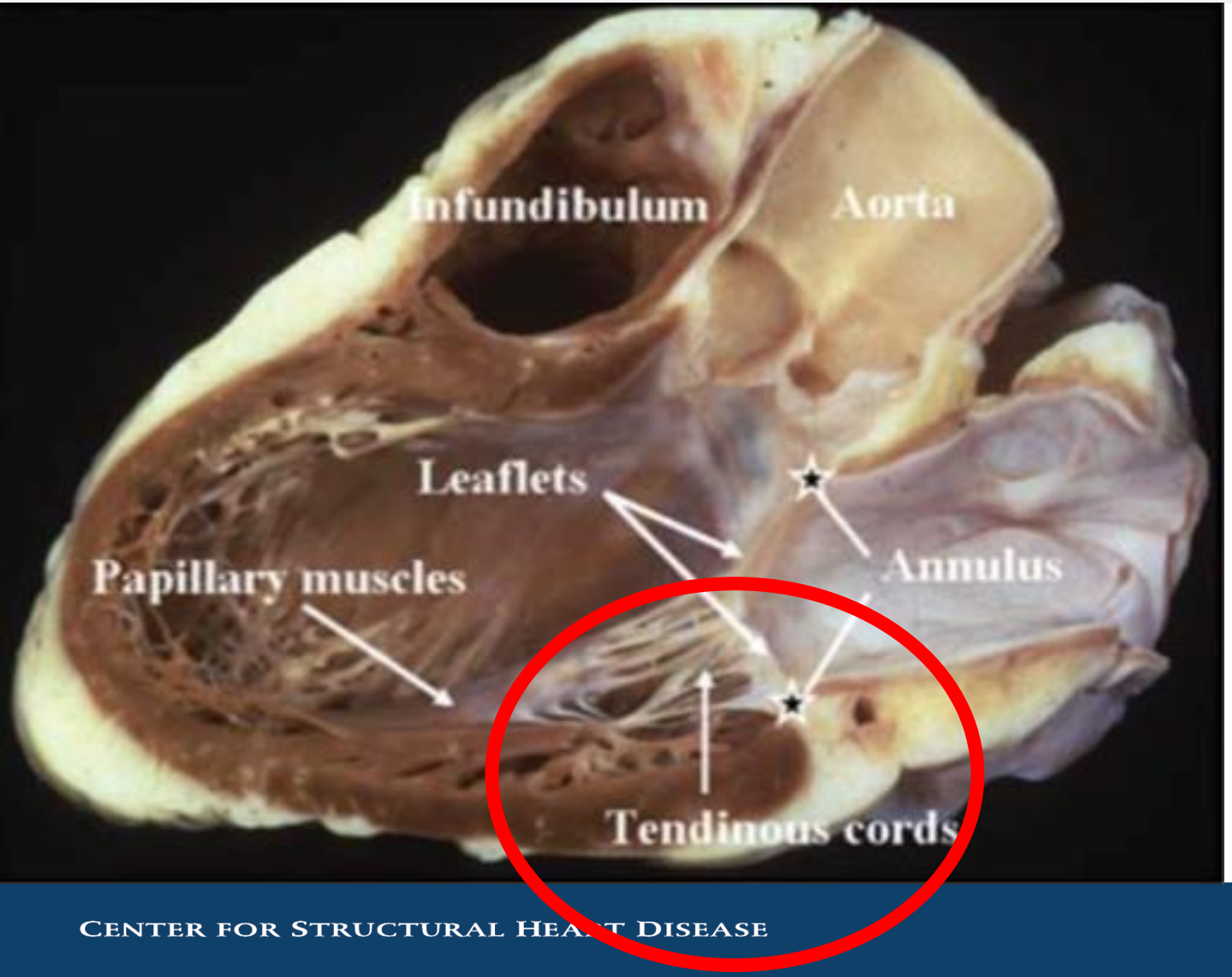
21 Patients – Paraguay & Brazil prior to BSX acquisition

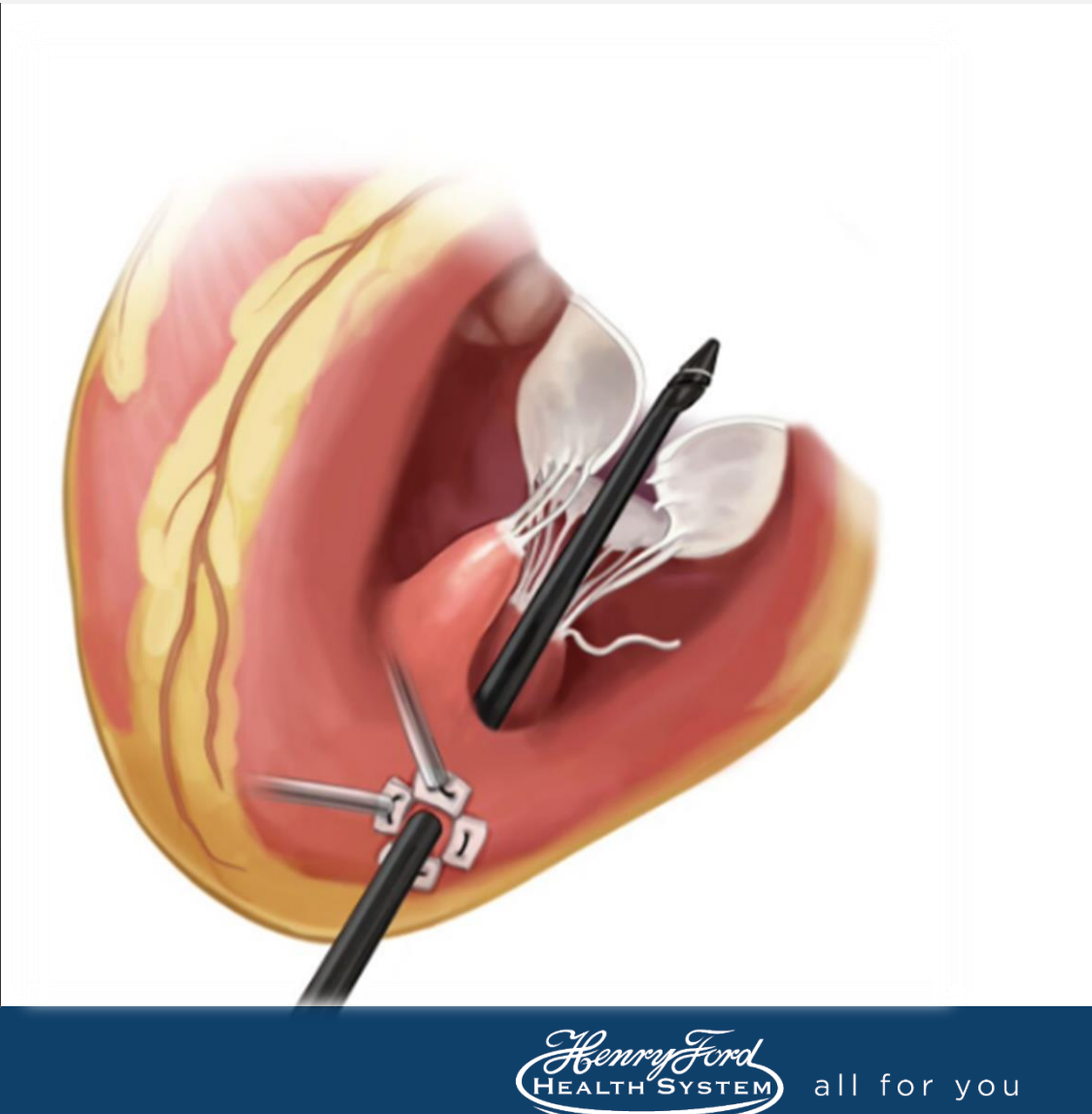
- 6 - 2017
- 15 - 2018 with integrated ICE
- No independent core lab review
- No 30 day mortality & few MAEs



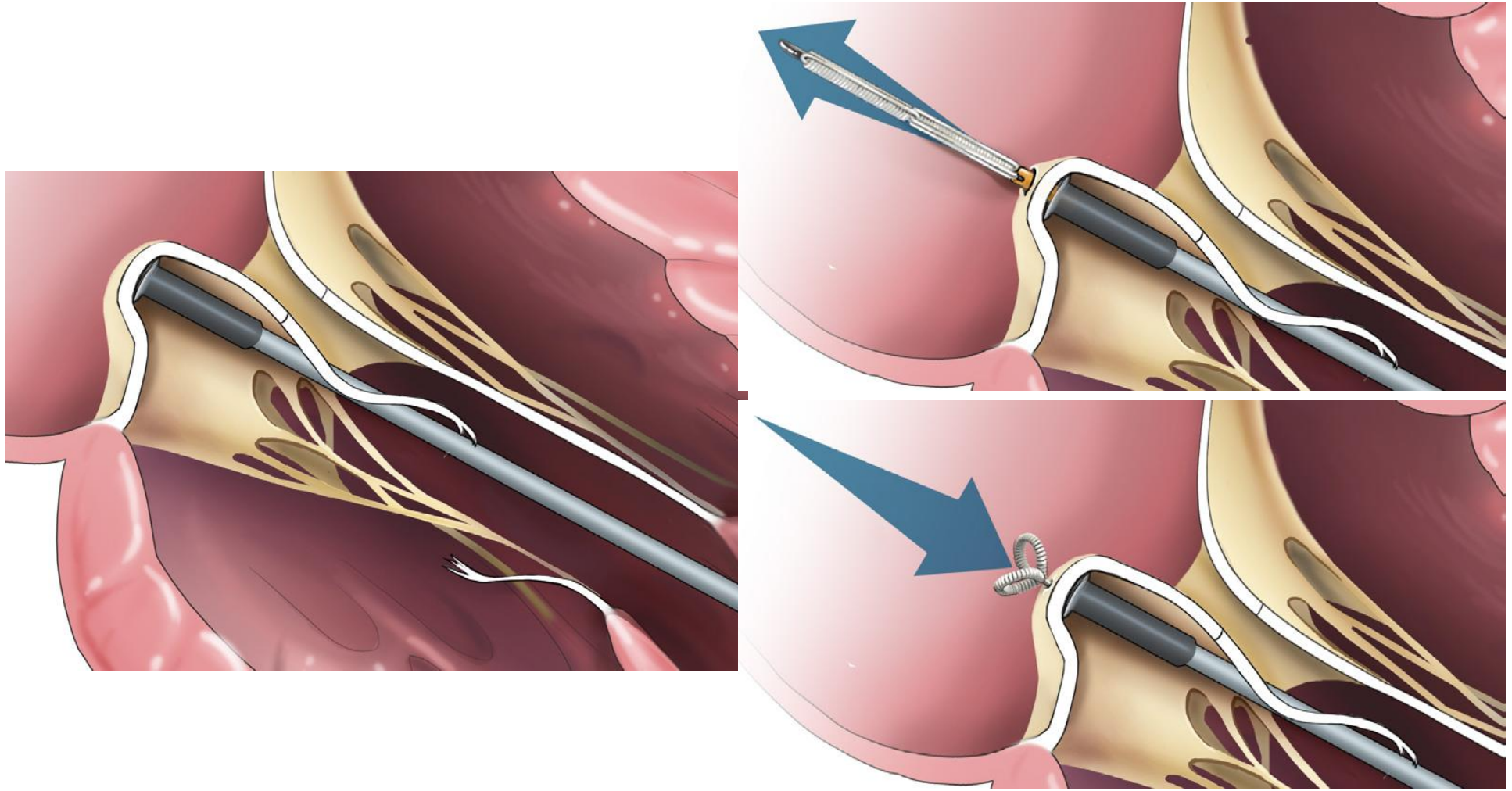


Chordal Repair for leaflet prolapse/flail



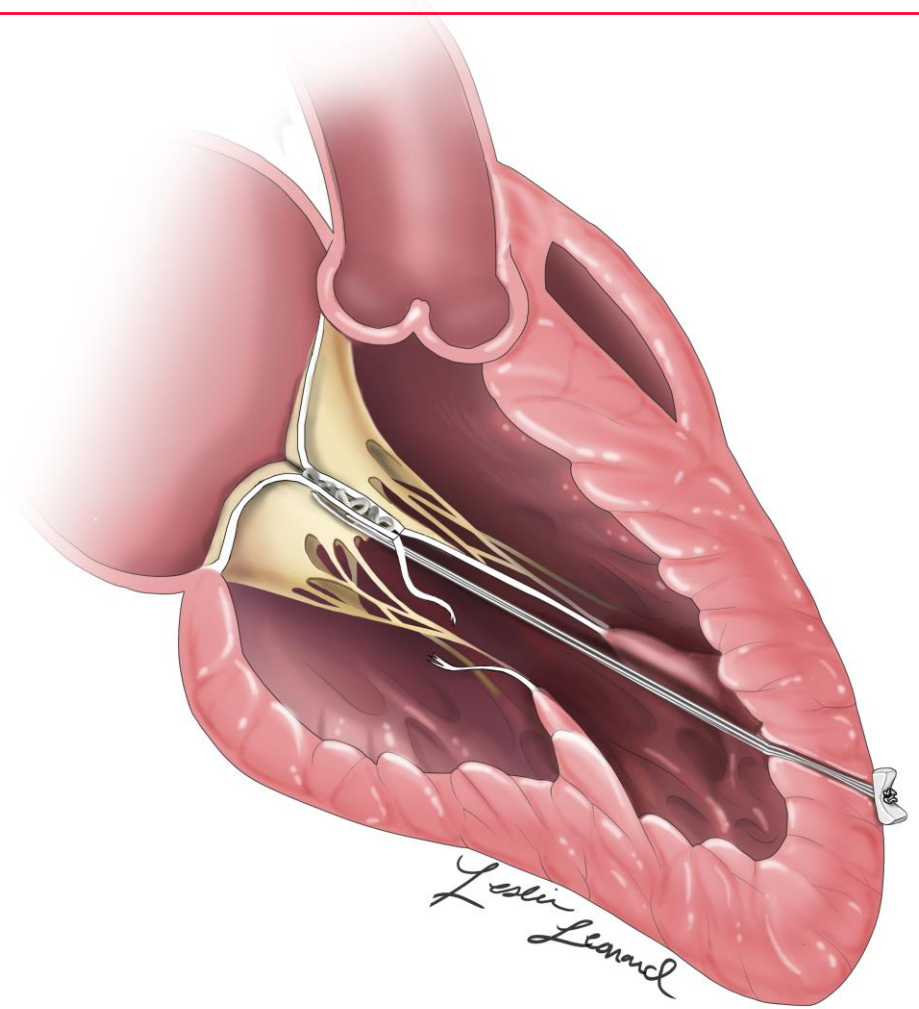


Harpoon Procedure



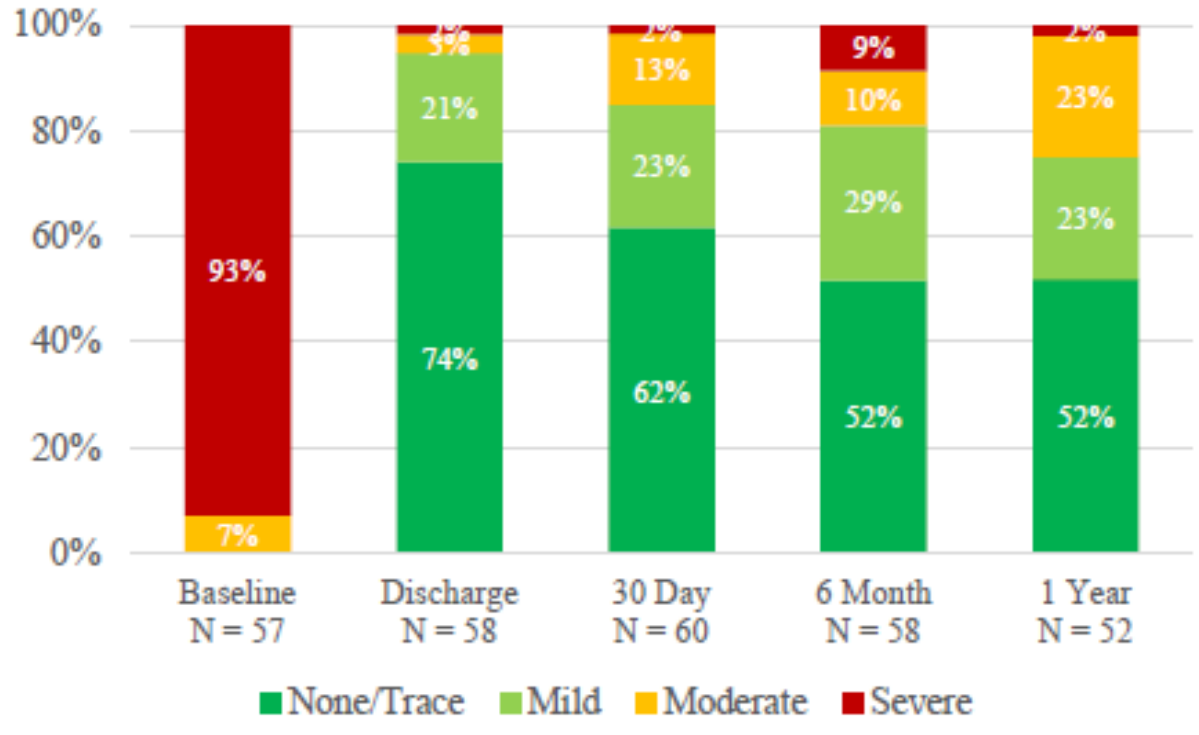
Gammie J TCT 2017

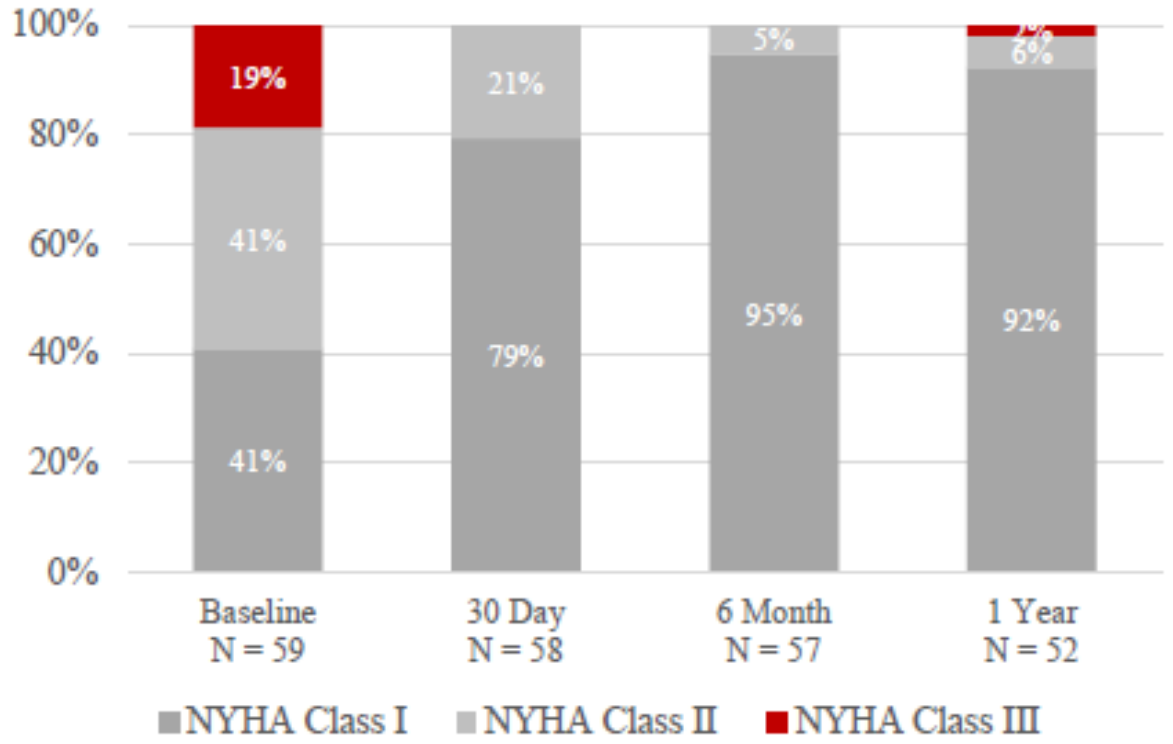
Real-Time Titration of ePTFE Cordal Length



Gammie J TCT 2017

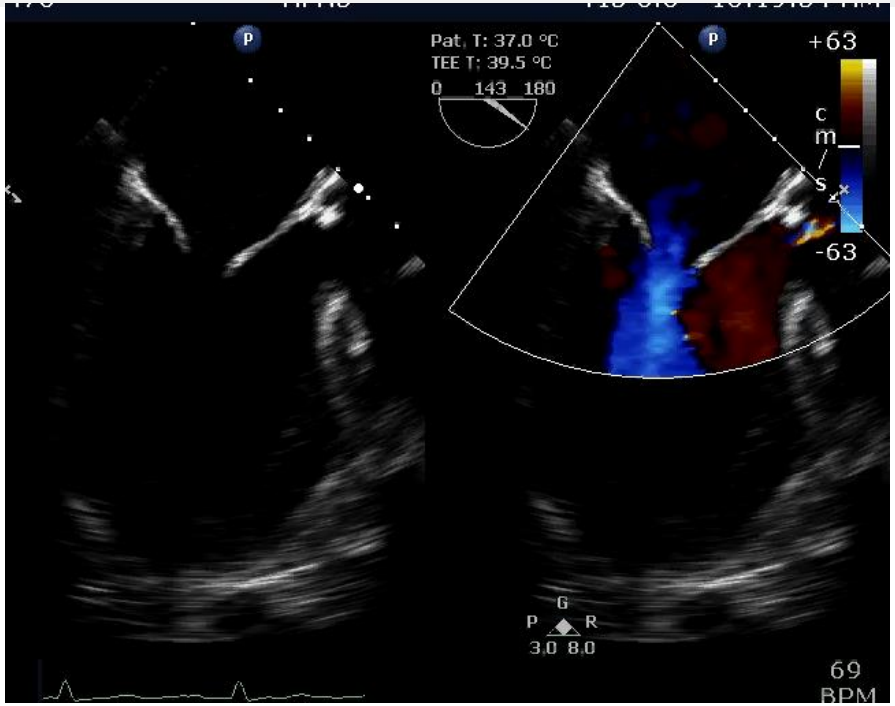
Harpoon
Early Feasiblity and TRACER CE trial





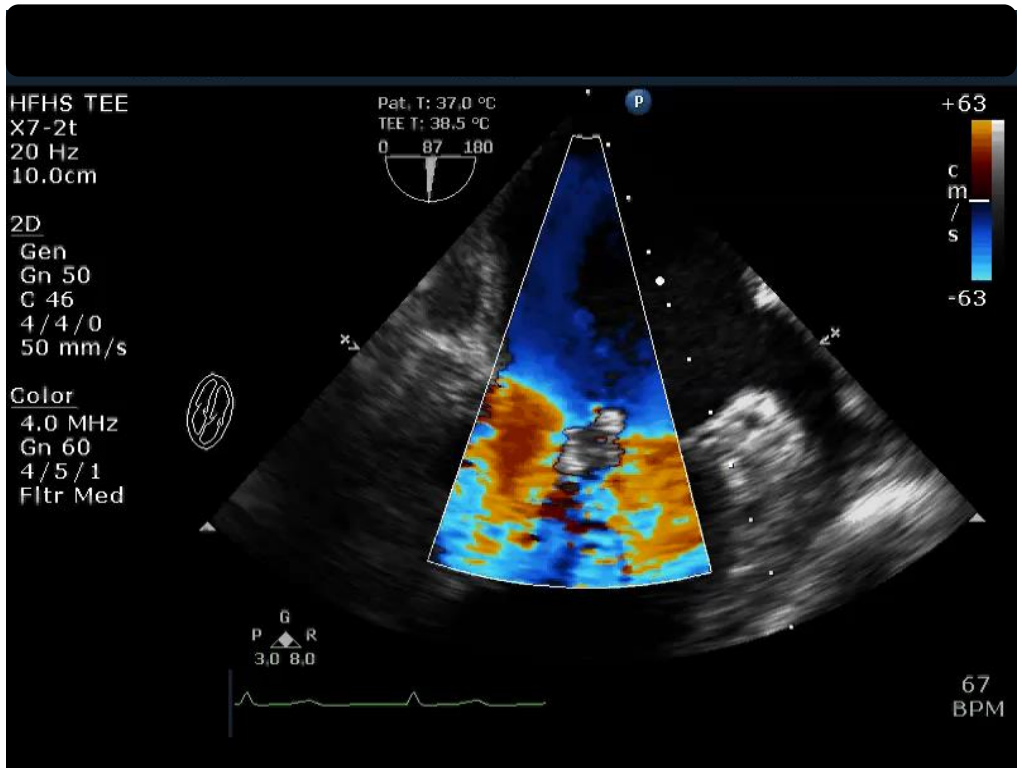
Summary

- Mitral Regurgitation increases as patients age
- Anatomy of the mitral is more complex
    - Requires more tools to fix
- Native and post-surgical
- 3 Main considerations
    - Anatomy
    - Etiology of mitral regurgitation (e.g. ischemic, prolapse)
    - Mechanism of failure

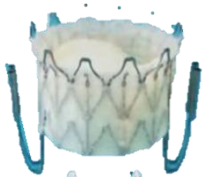


Summary

- Treatment of Functional Mitral Regurgitation
  - COAPT Proved MR reduction in Cardiomyopathy improves outcomes
  - Mortality, HF hospitalizations, symptoms, QOL
- Many tools for repair based anatomy
  - Leaflet repair
    - Edge-to-edge
      - Focal jets
      - Flail segment
  - Annulus
    - Cardioband
    - Millipede
    - Cerclage
  - NeoChords



Transcatheter mitral valves
Sampling



SATURN
TMVR

Braile
Biomedica

Braile
Biomedica

Sapien M3
Edwards

CardiAQ
Edwards

Cephea

Mitraltech

Direct Flow
Medical

Twelve
Medtronic

M-Valve

Edwards
Fortis

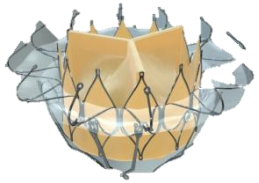
HighLife

Caisson

Navigate

Neovasc
Tiara

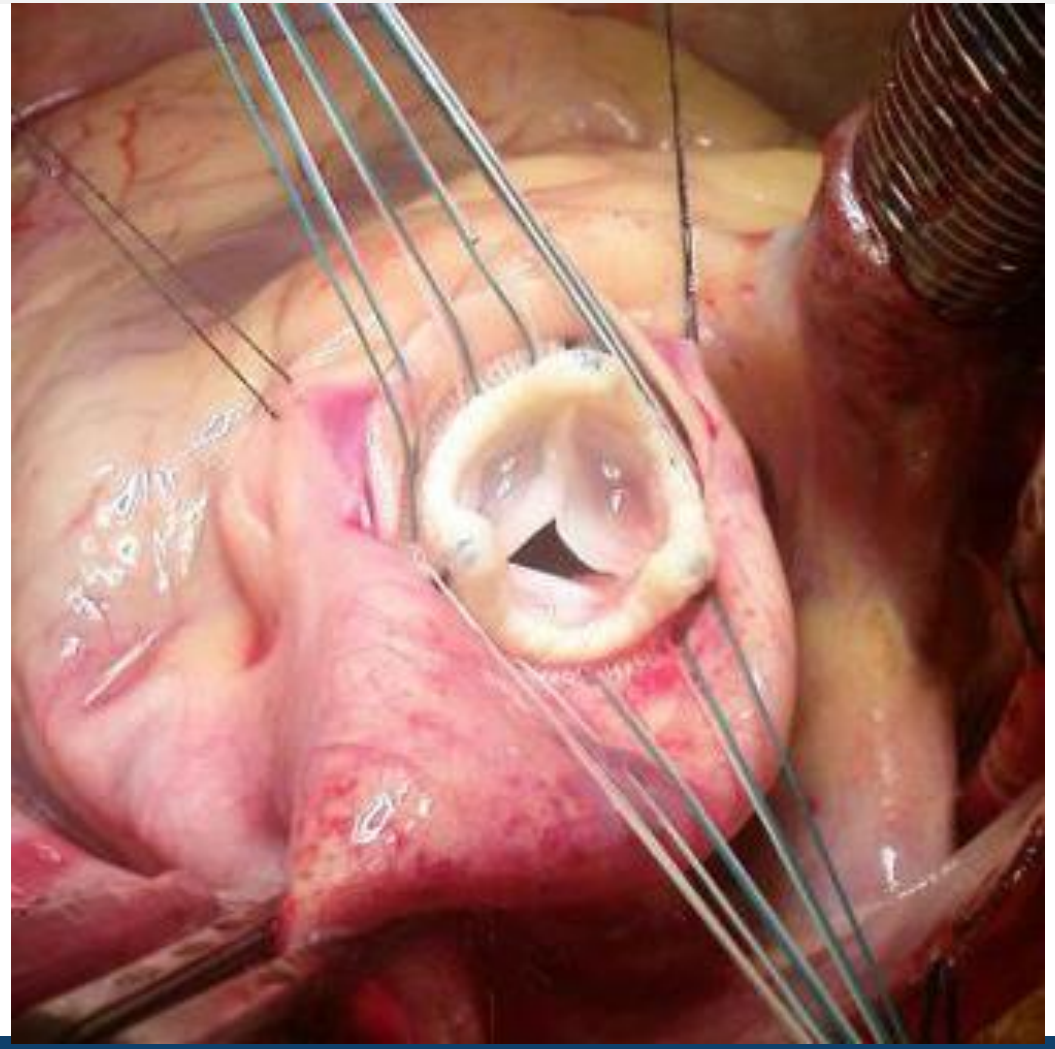
PermaValve
MID



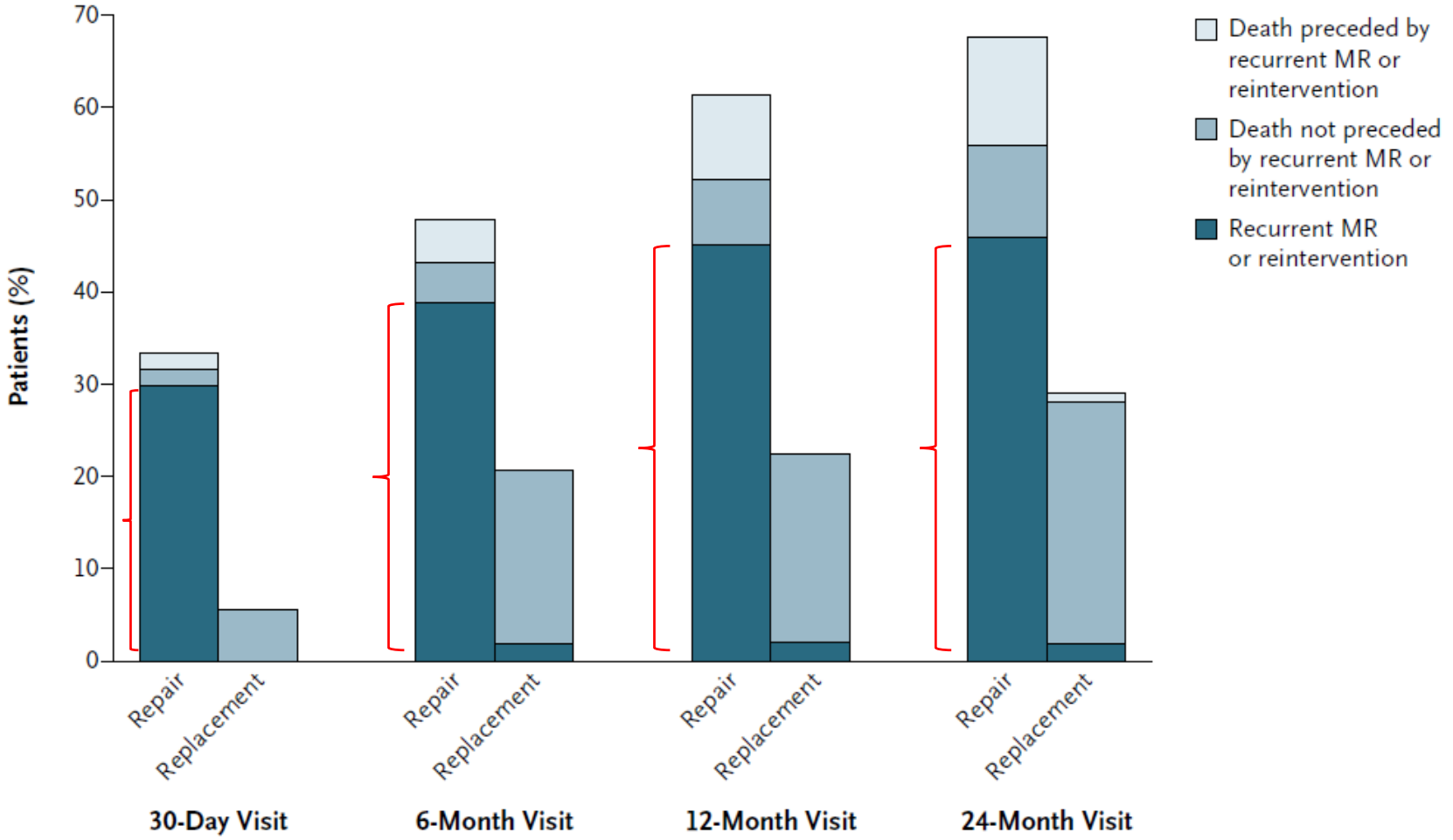
Sinomed

Tendyne
Abbott

Replacement
Does it offer advantages?

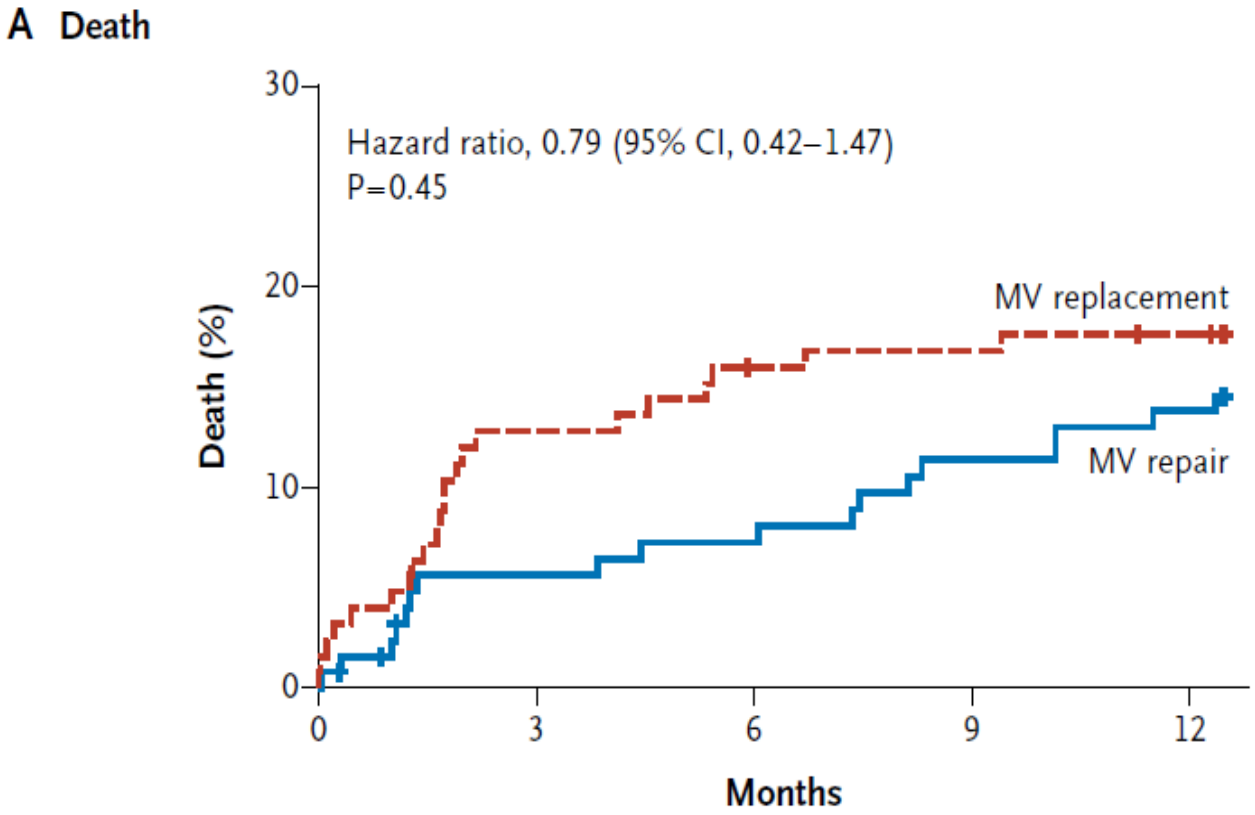


Repair in Functional MR (Ischemic) Prone to Recurrent MR



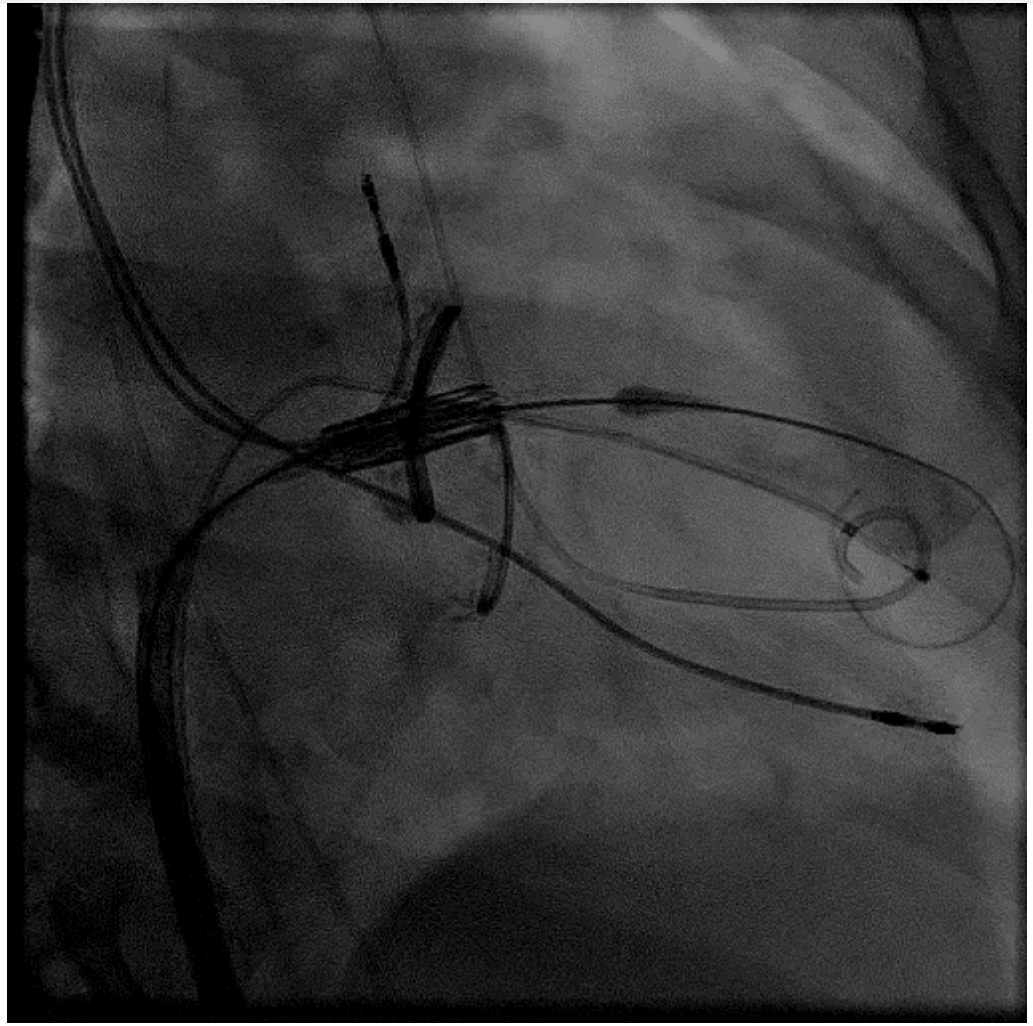
Goldstein D et al. N Engl J Med 2016;374:344-53.

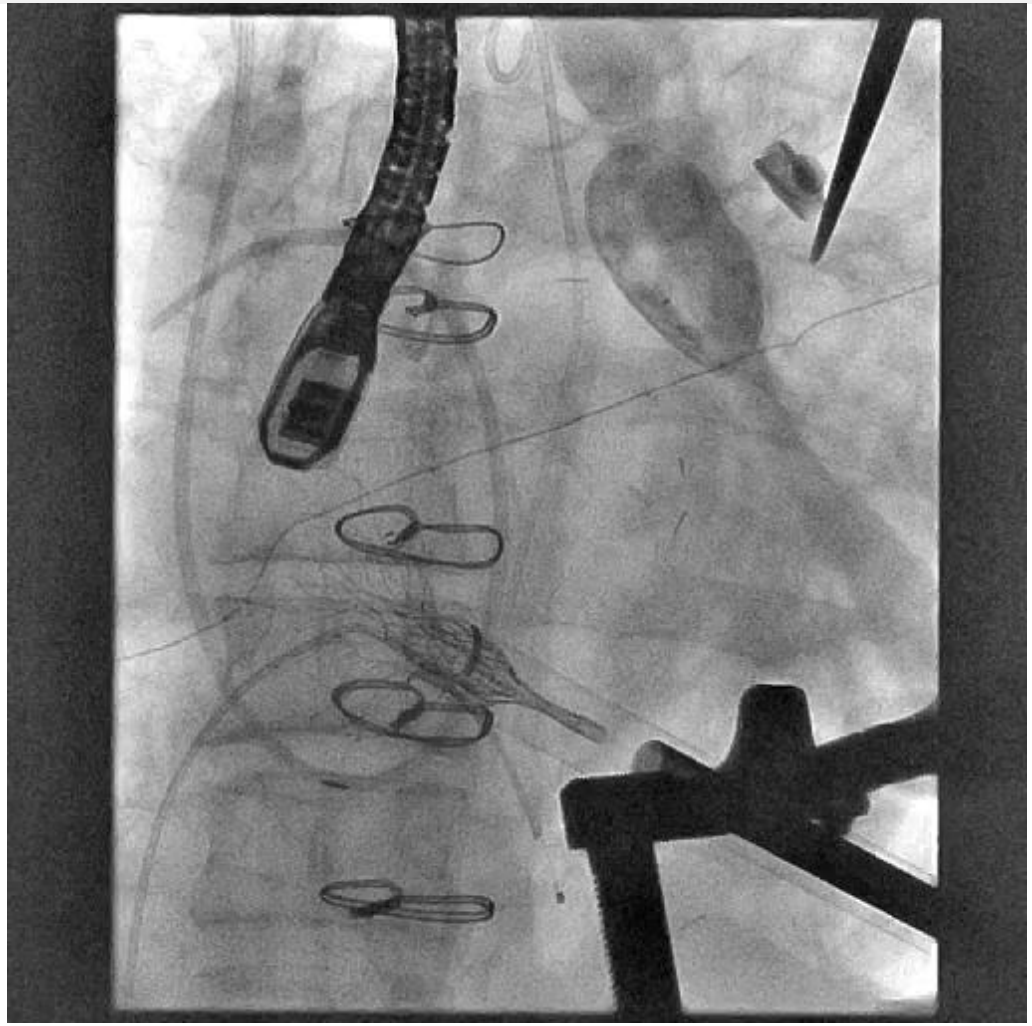
Mitral Valve Replacement in ICM
Higher Early Mortality Compared to Repair



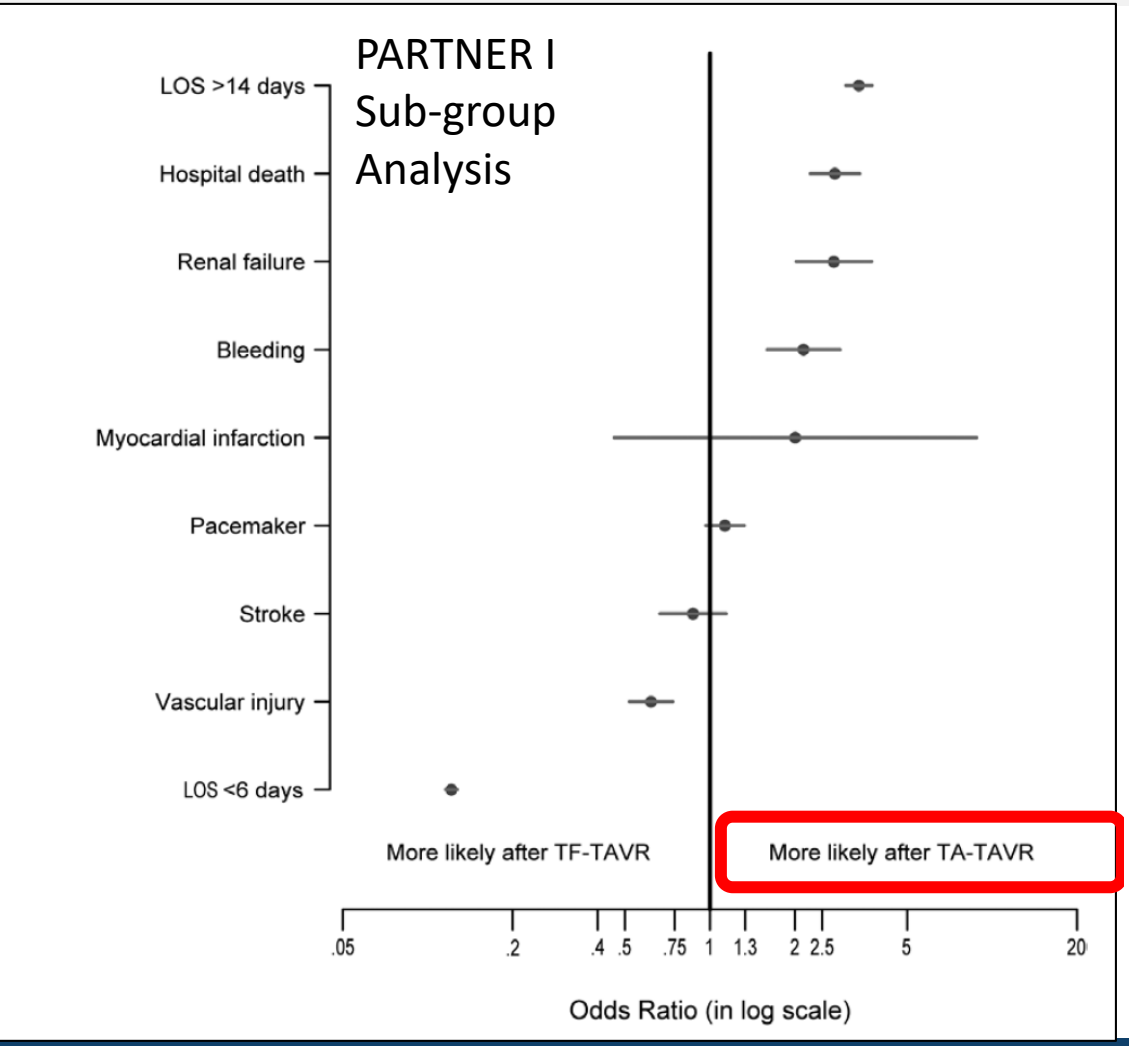
Acker MA et al. N Engl J Med 2014;370:23-32.

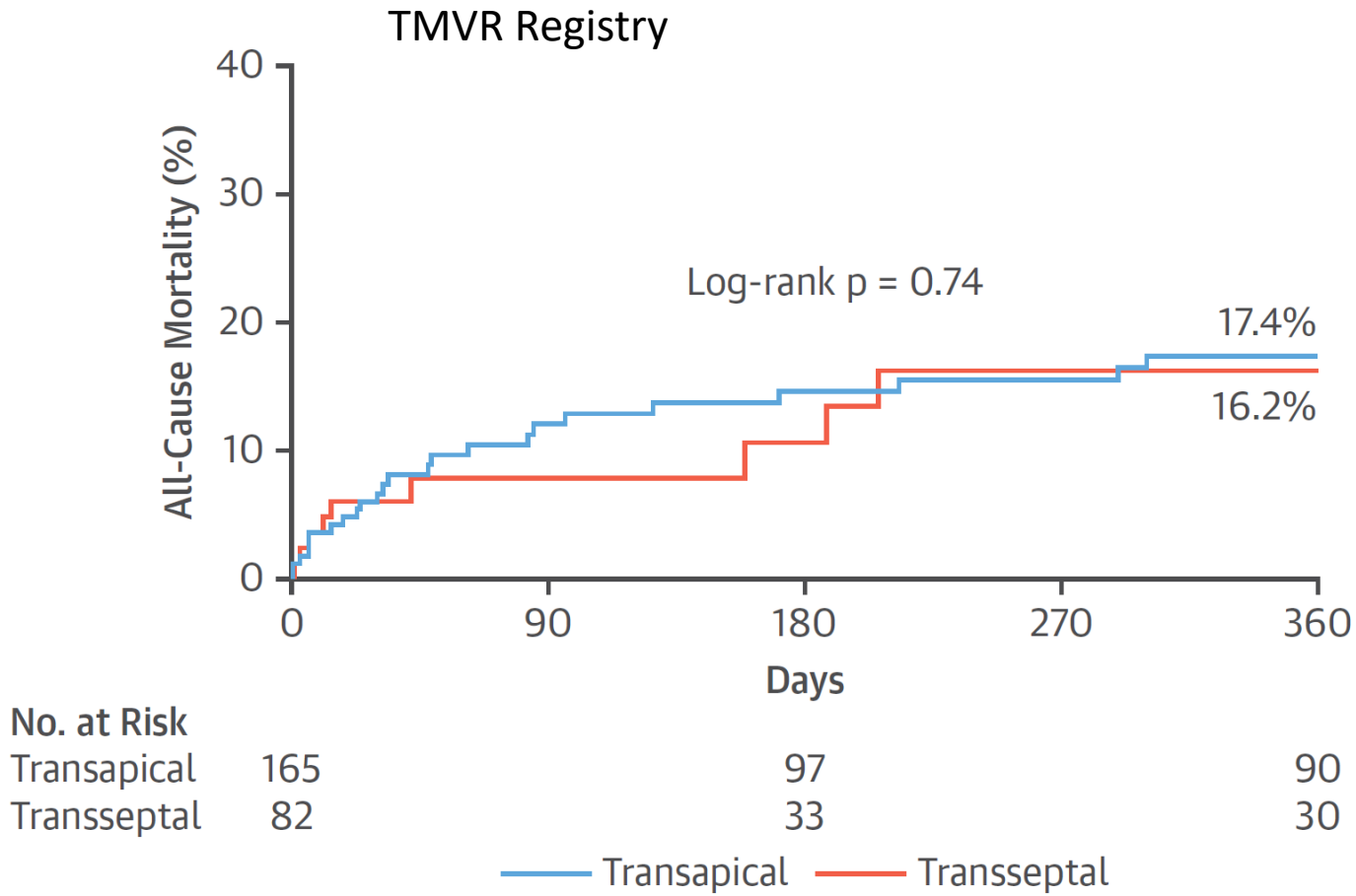
Transseptal vs. Transapical





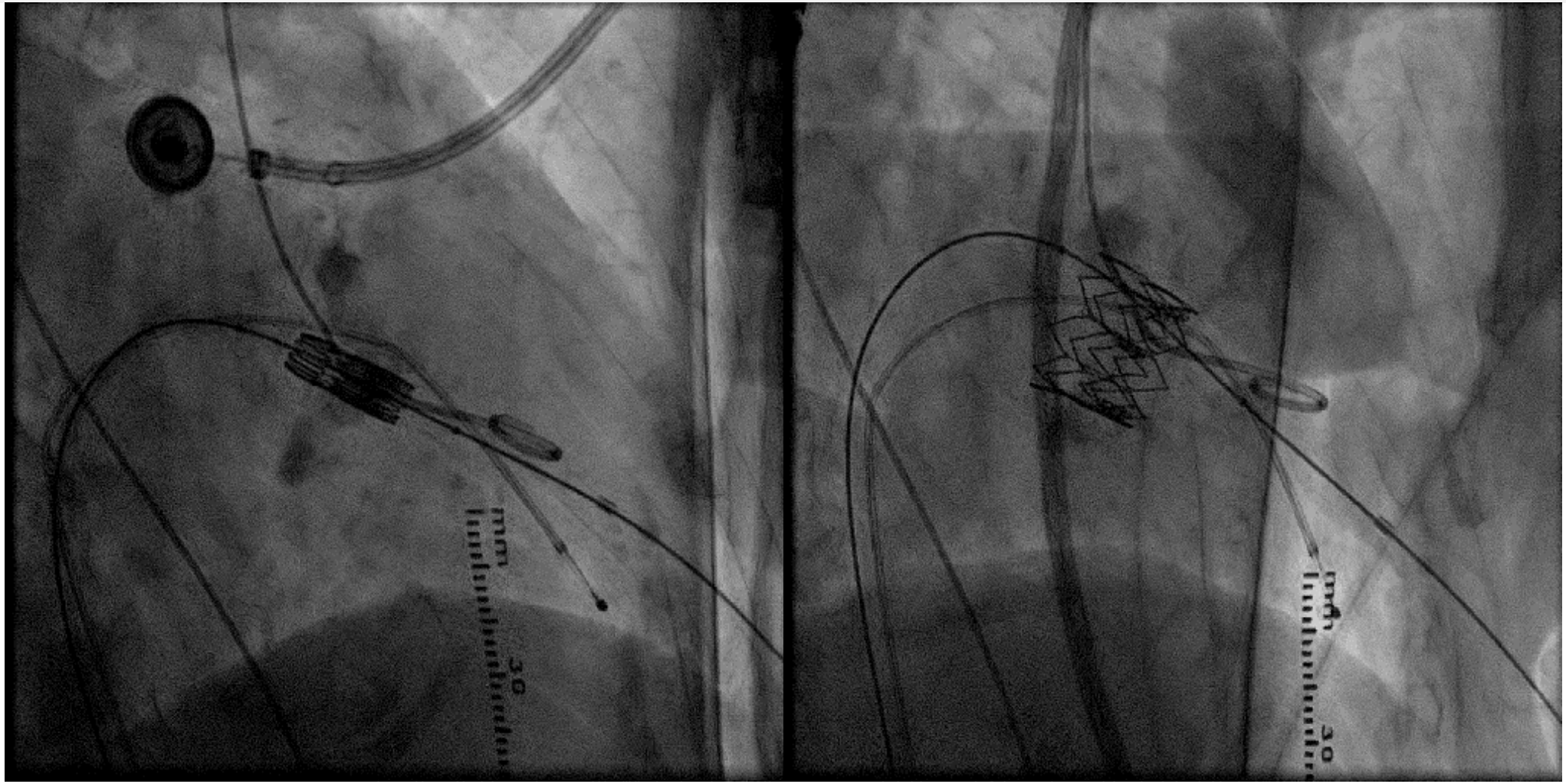
Transseptal vs. Transapical



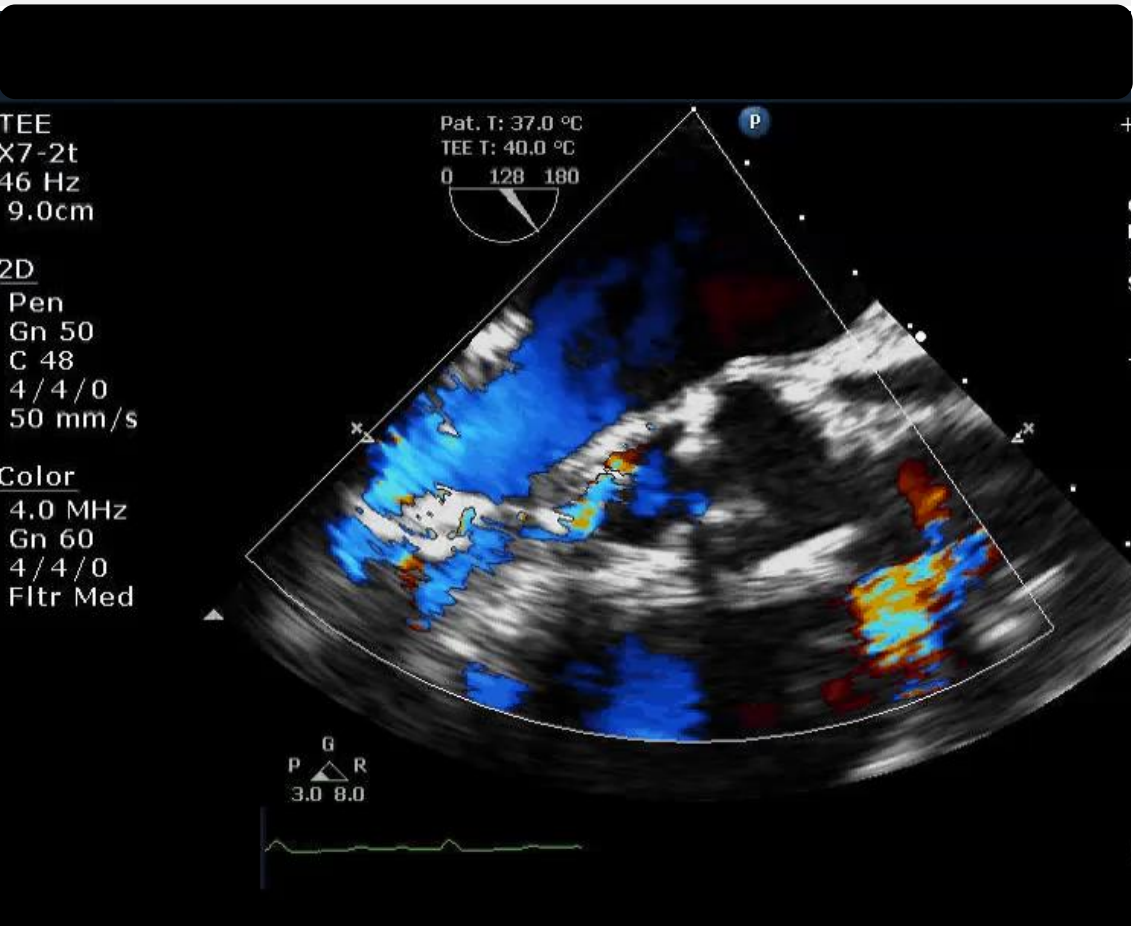


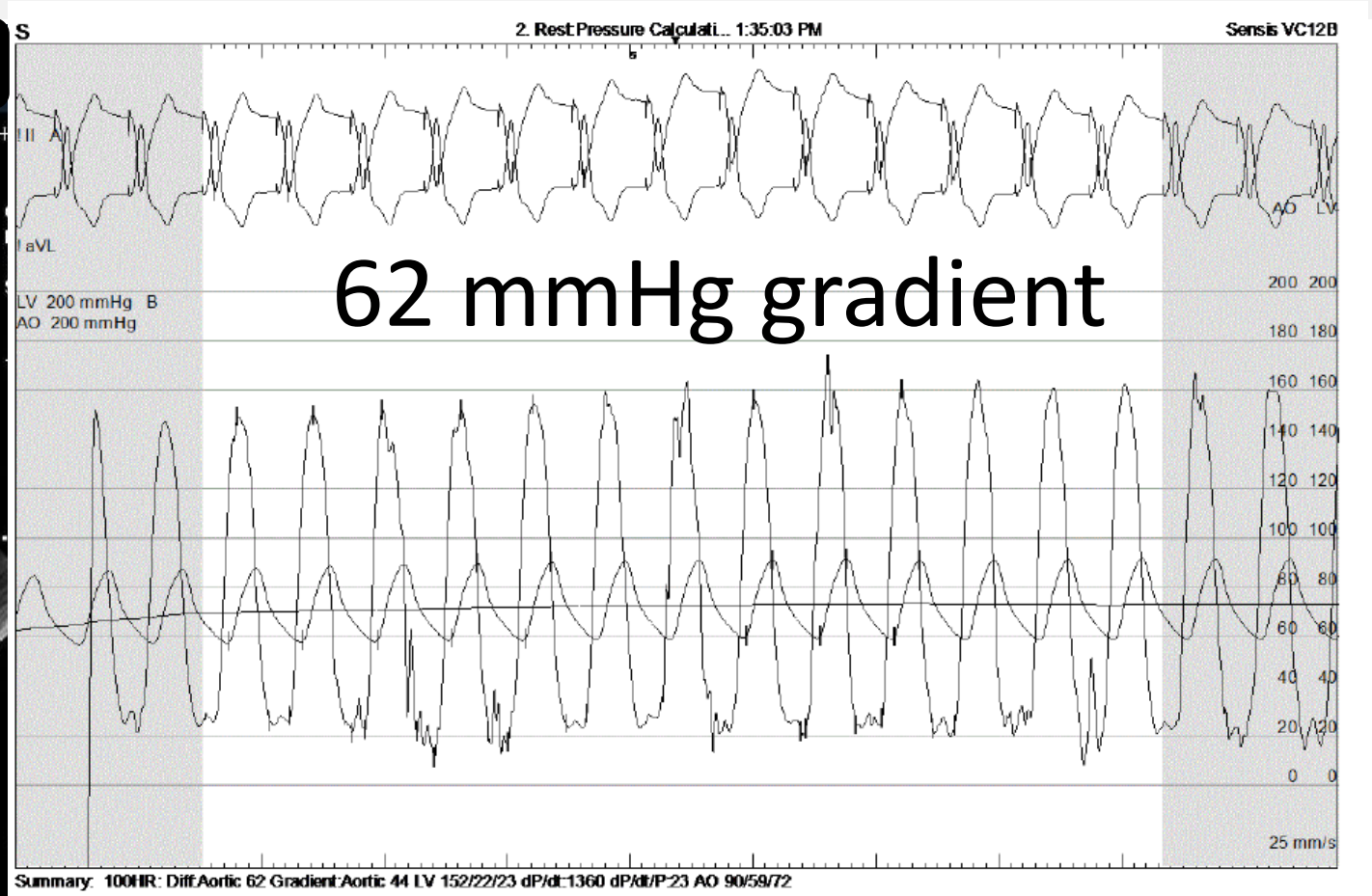
Blackstone E Circulation 2015;131:1928-00.
Yoon S et al. JACC 2017;70:1121-31.

88 yo F with calcific mitral stenosis

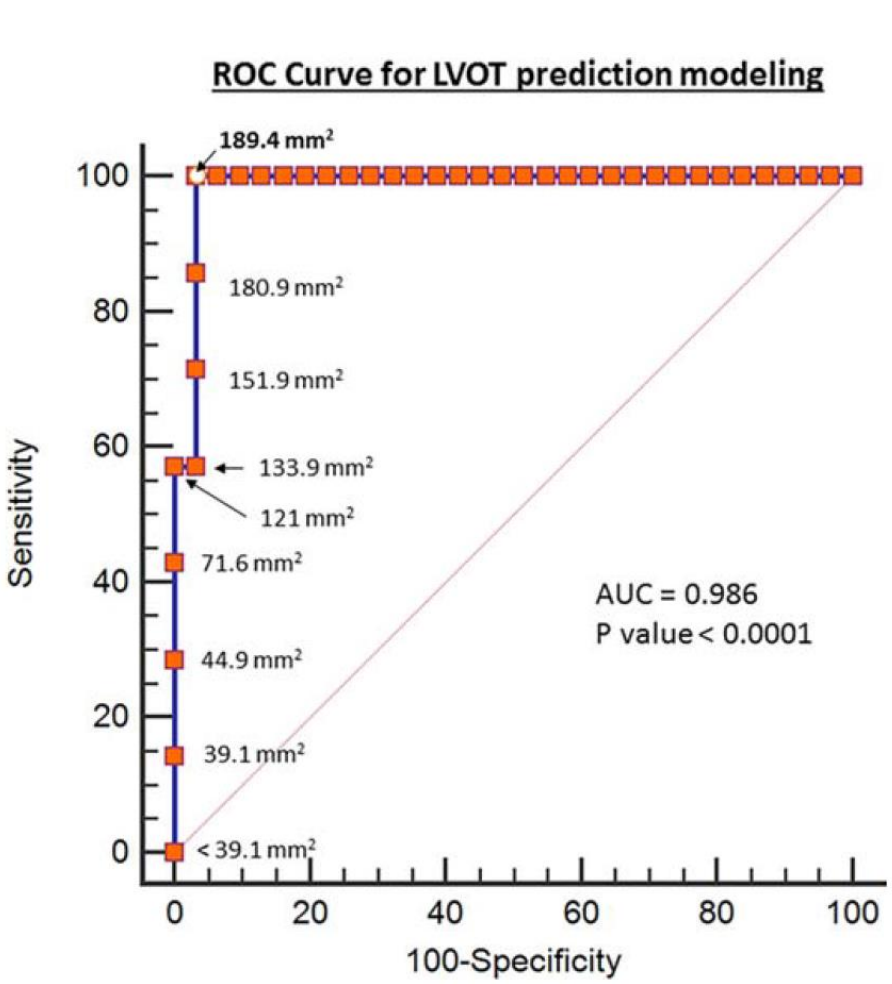


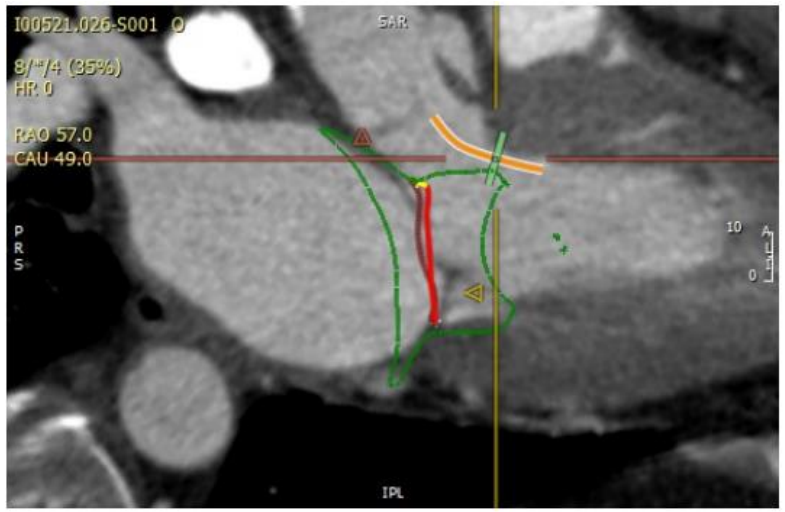
Recovery after a PEA arrest

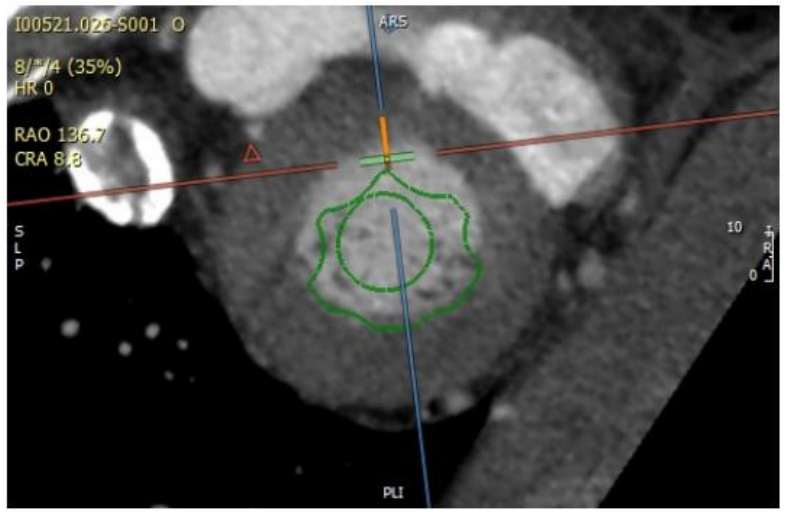


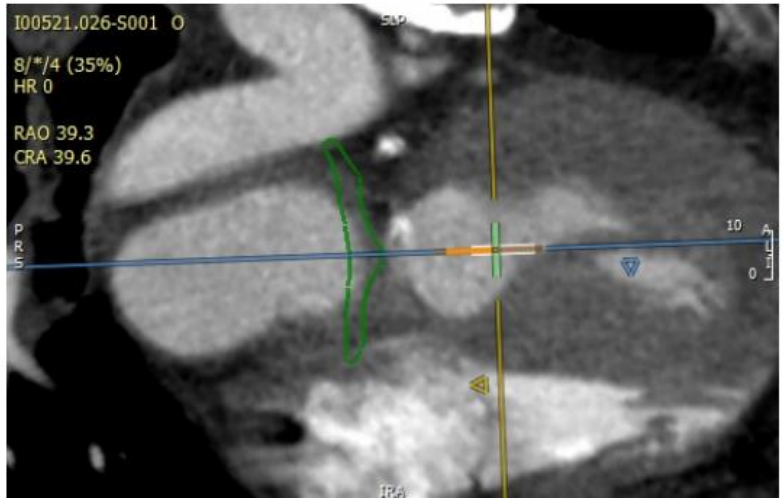


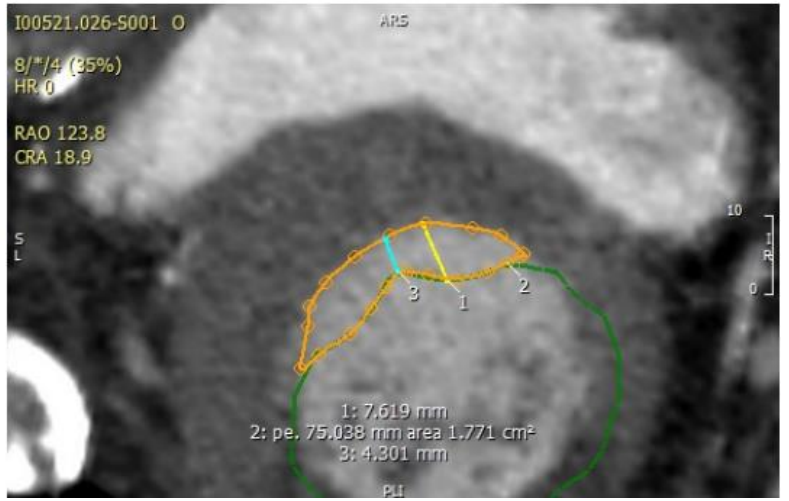
When do we obstruct?







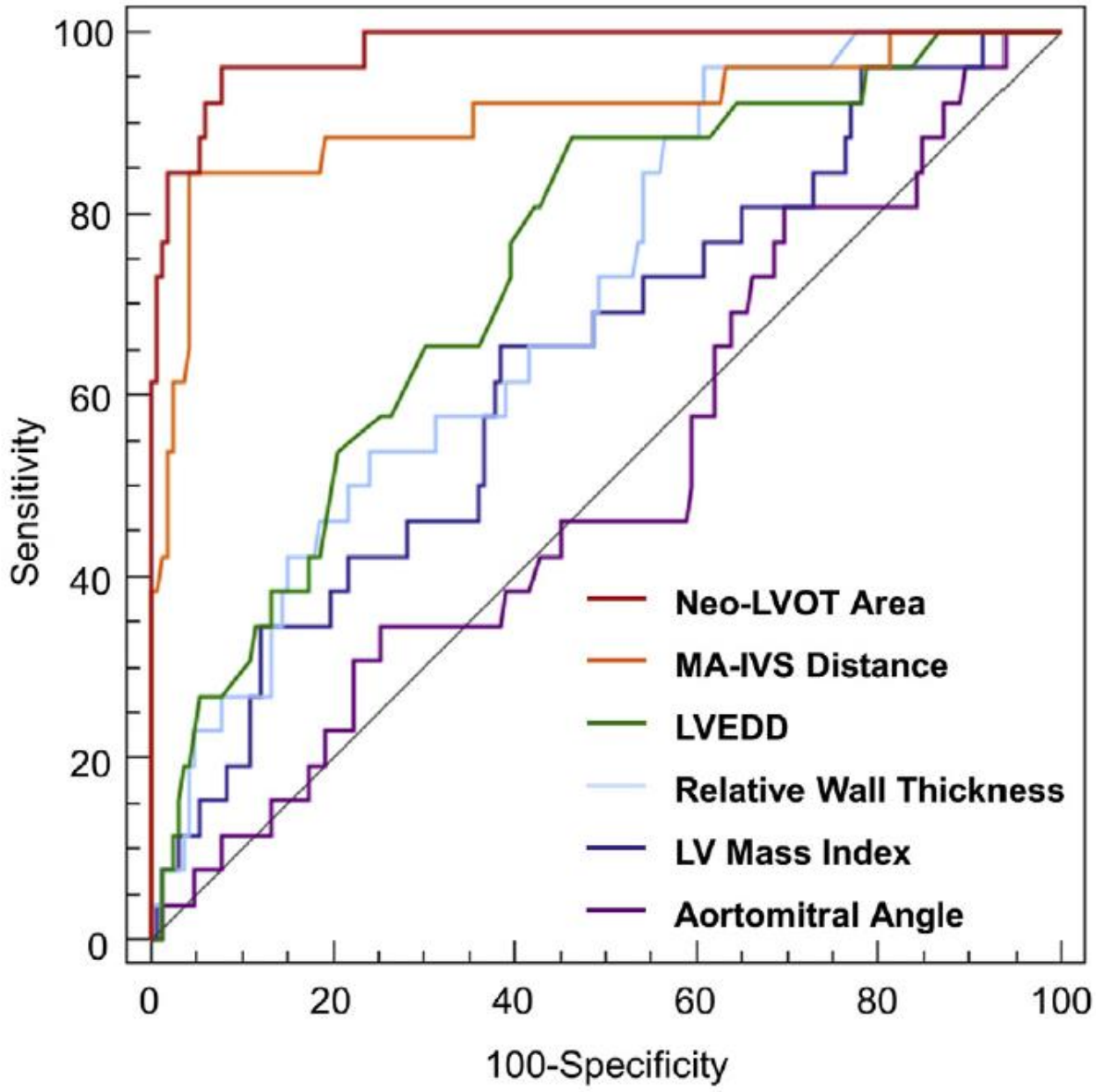




Wang DD et al. CCI 2017

ROC
LVOT Obstruction

- Neo-LVOT 170 mm2
  - Sensitivity 96.2%
  - Specificity 92.3%
- MA-IVS
  - Sensitivity 84.6%
  - Specificity 95.8%



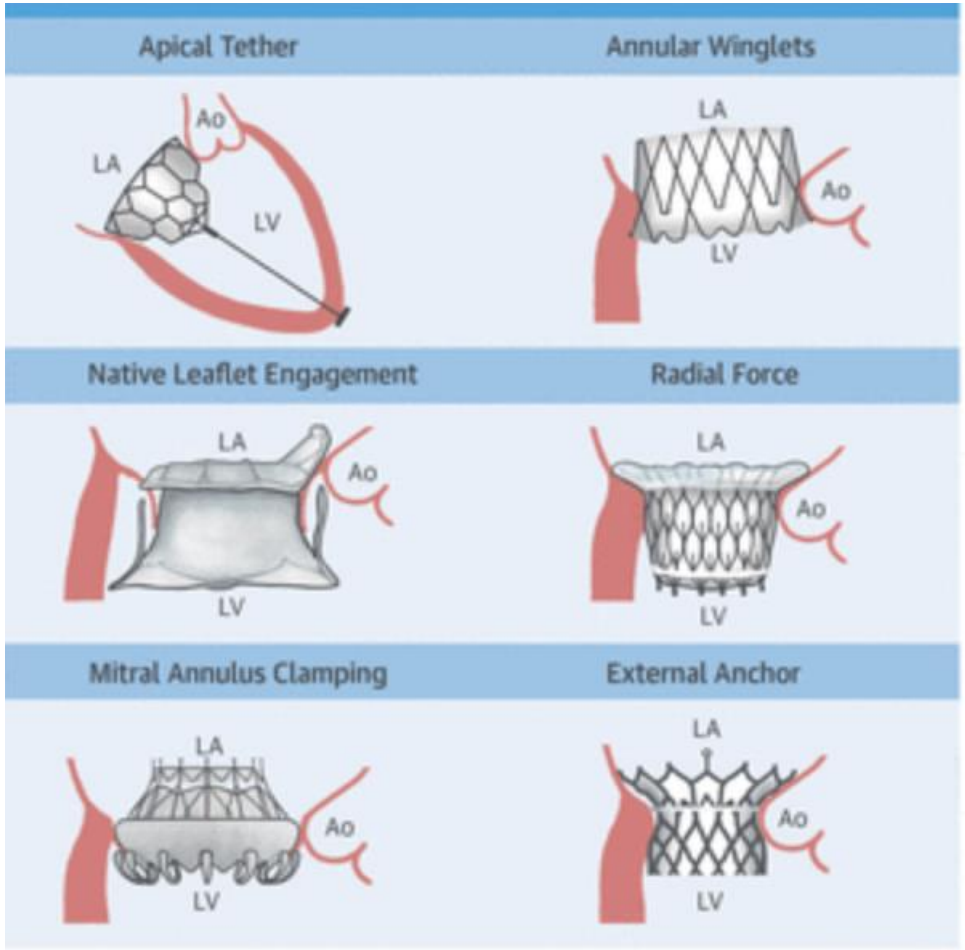
Yoon SH JACC Int. 2019;12:182-93.

Specific valve sizes and fixation mechanisms
High rate of anatomic screen failure

Enrolled
N = 332 Enrolled
N = 100 Treated

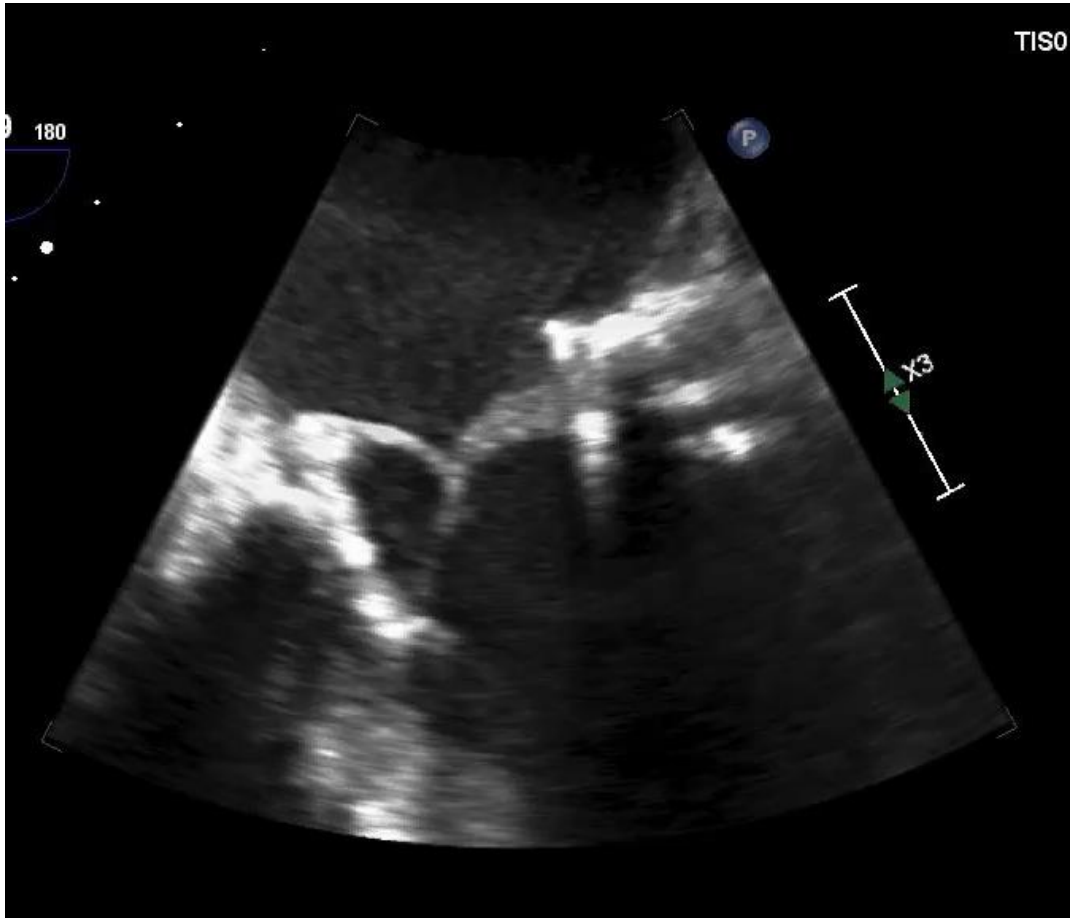
Screen fails: 212
On hold: 13
Pending decision or awaiting treatment: 7

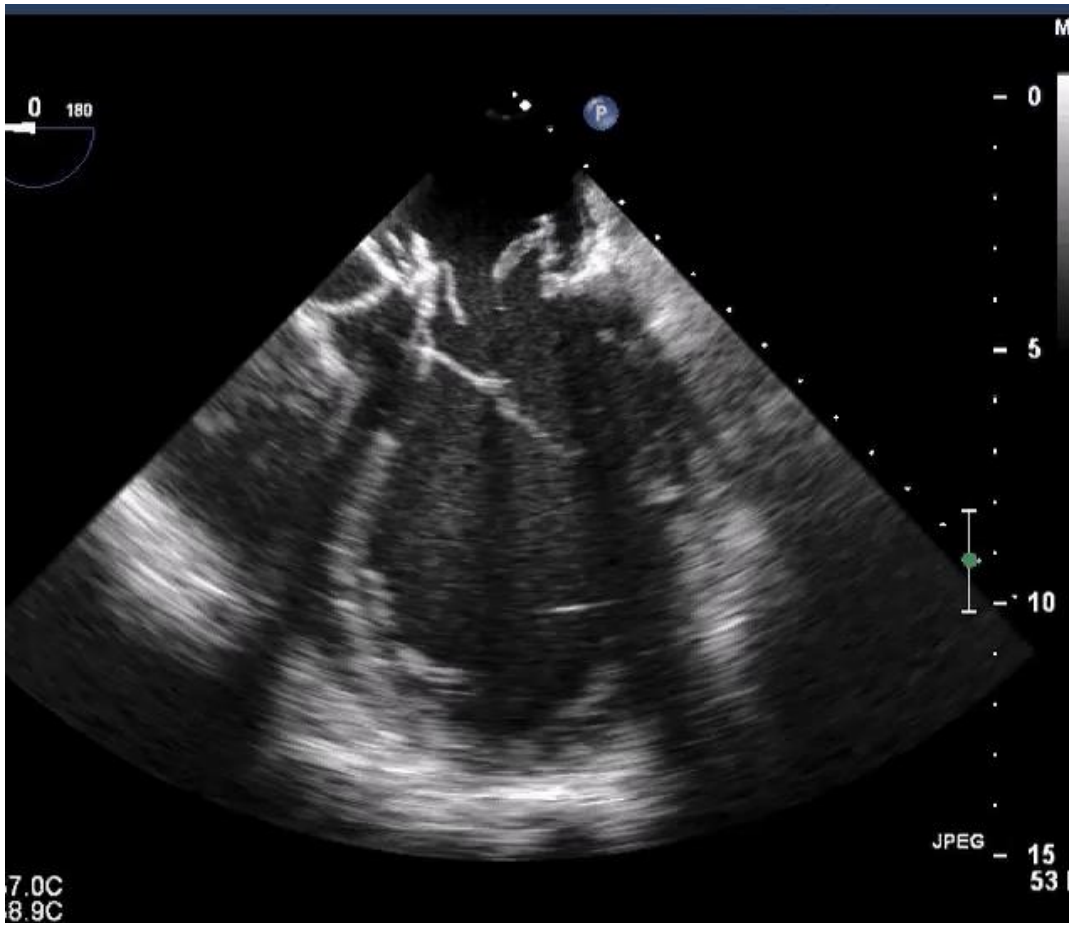
Baseline Evaluation
N = 100
# Followed at Visit: 100



Ragueriro, A. et al. J Am Coll Cardiol. 2017,69(17) 2175-92
Sorajja P et al JACC 2019;73:1250.

Need for anticoagulation Duration?

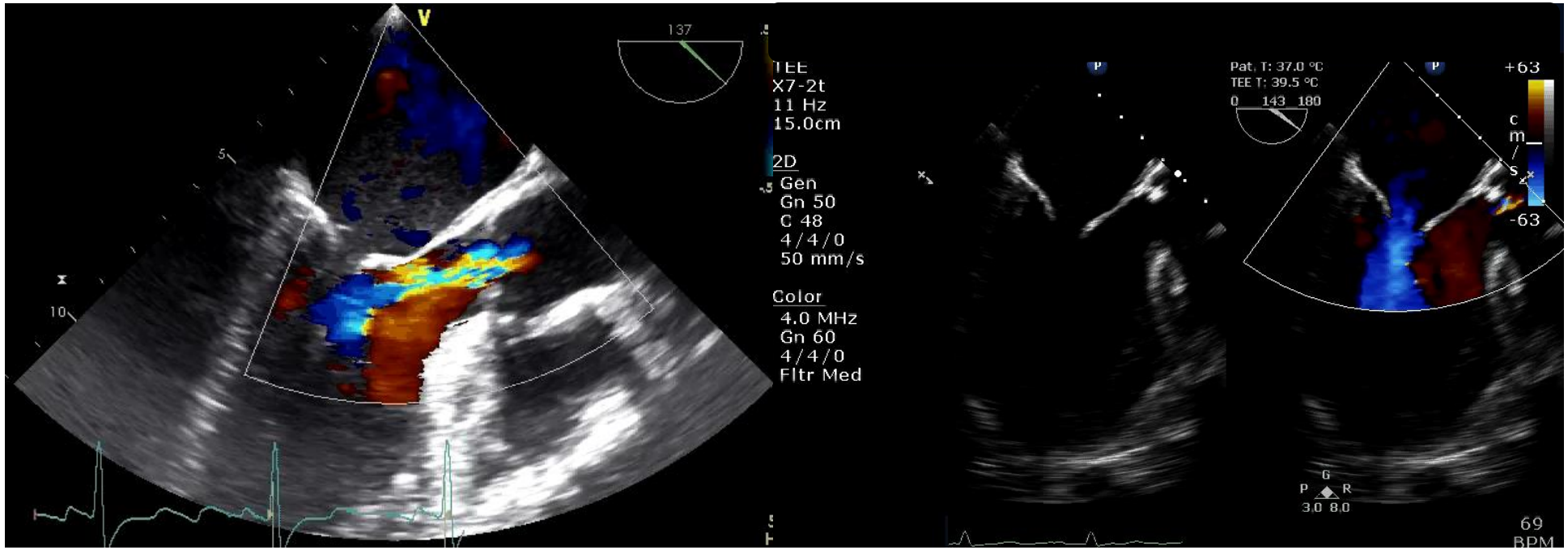




History

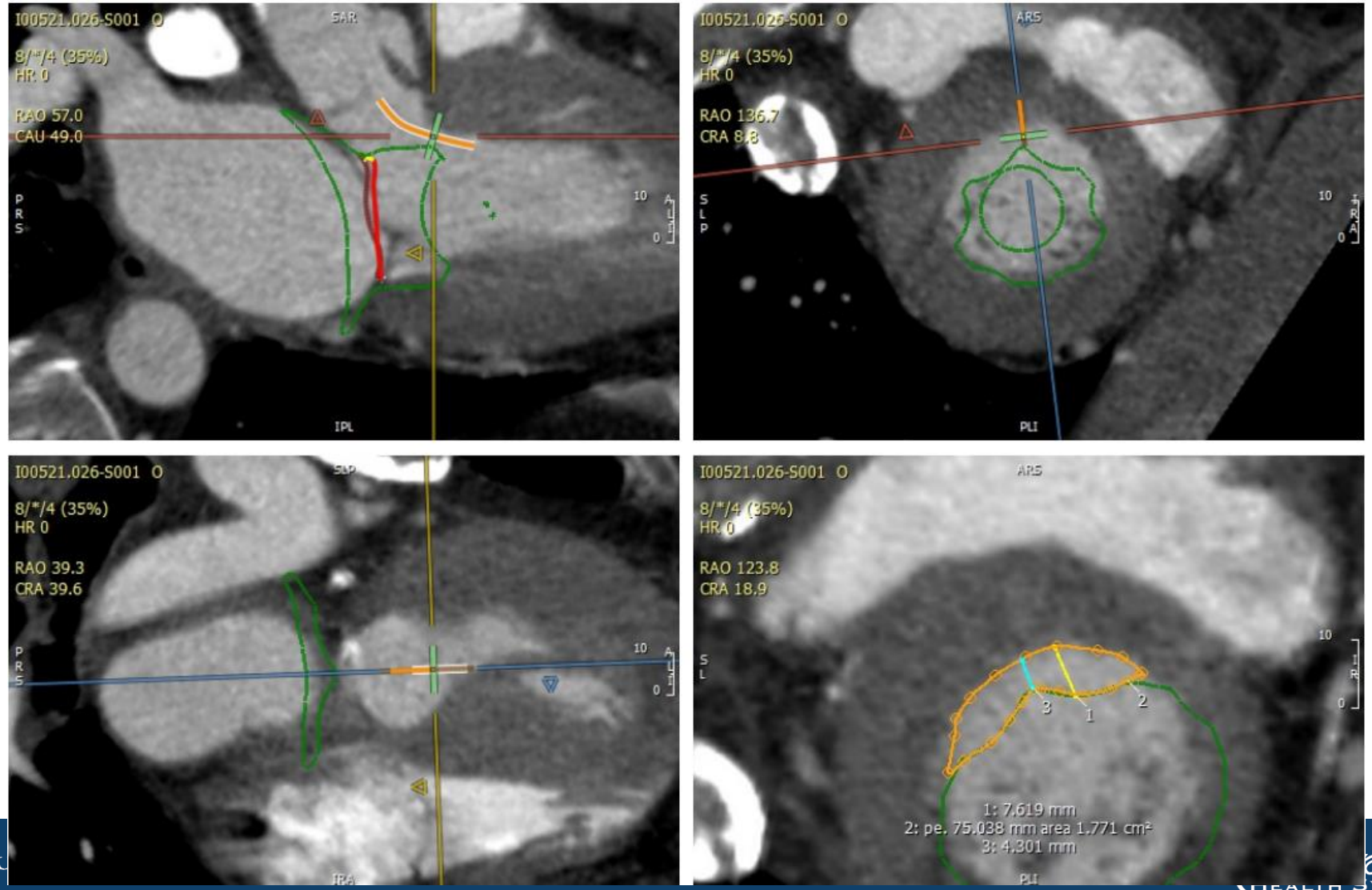
- 55 yo M NYHA III
  - Severe Mitral Regurgitation
    - Functional
  - Moderate-Severe Aortic Insufficiency
  - Prior hx non-Hodgkin's Lymphoma
    - mantle radiation
  - Prior CABG (LIMA, SVG-OM)
- Repeat sternotomy
  - Aborted AVR/MVR due to hostile chest
- Evaluation for percutaneous treatment

TMVR- Functional MR

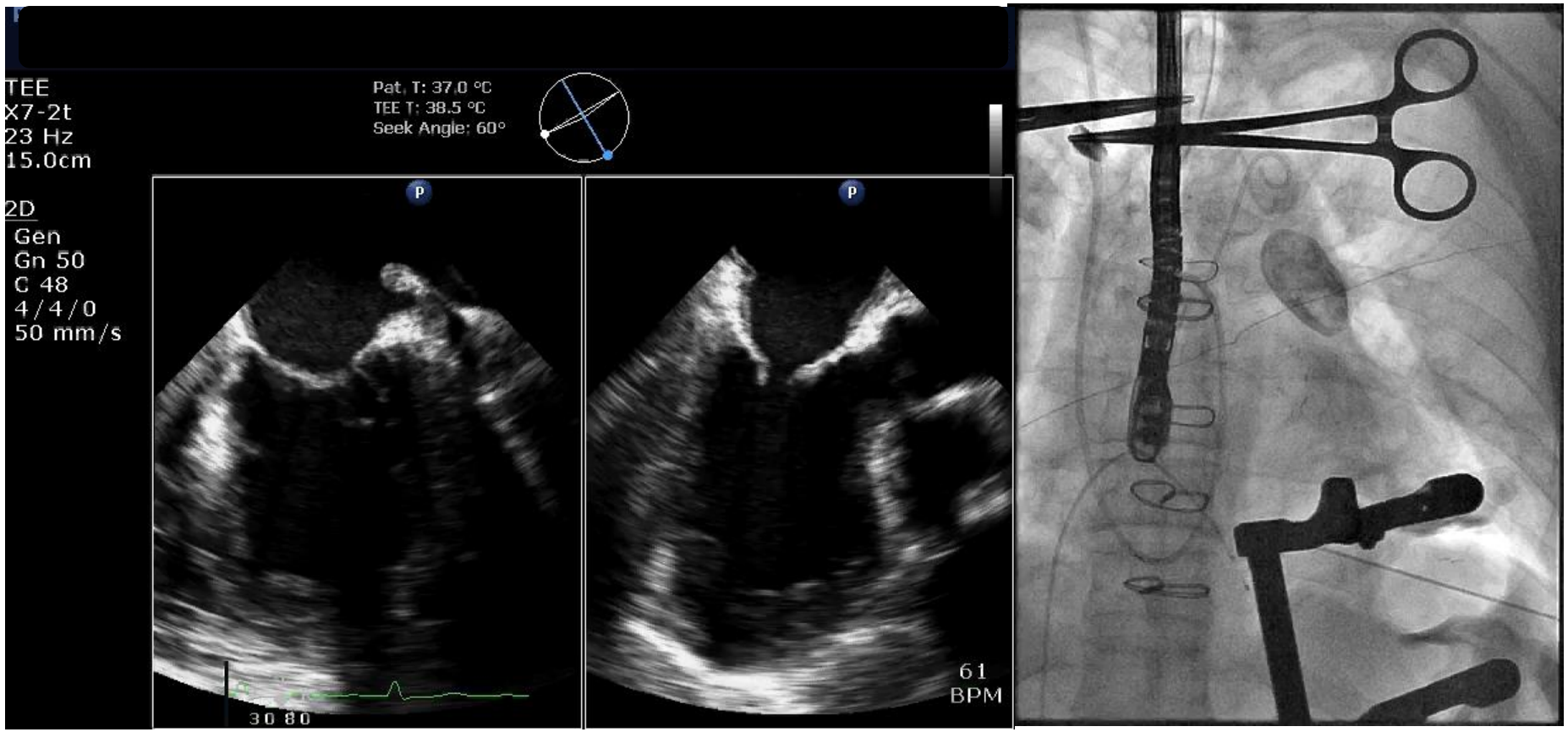


TMVR- Functional MR
Neo-LVOT Measurement

Courtesy of J. Leipsic and P. Blanke



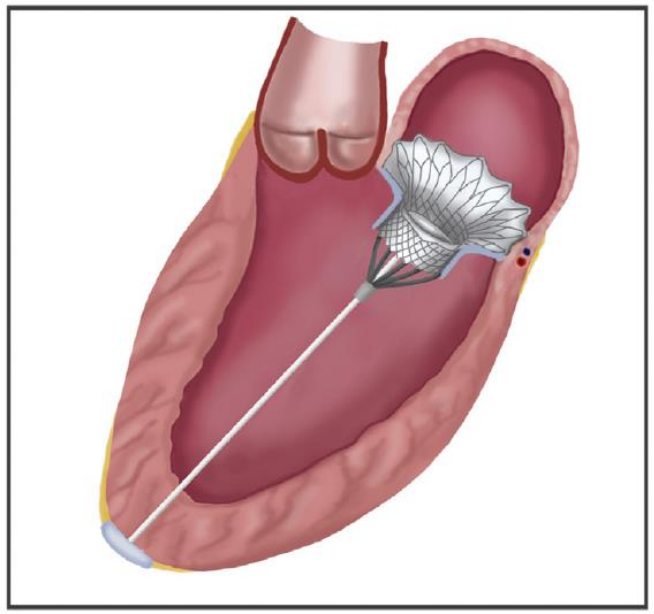
TMVR- Functional MR
Apical Access



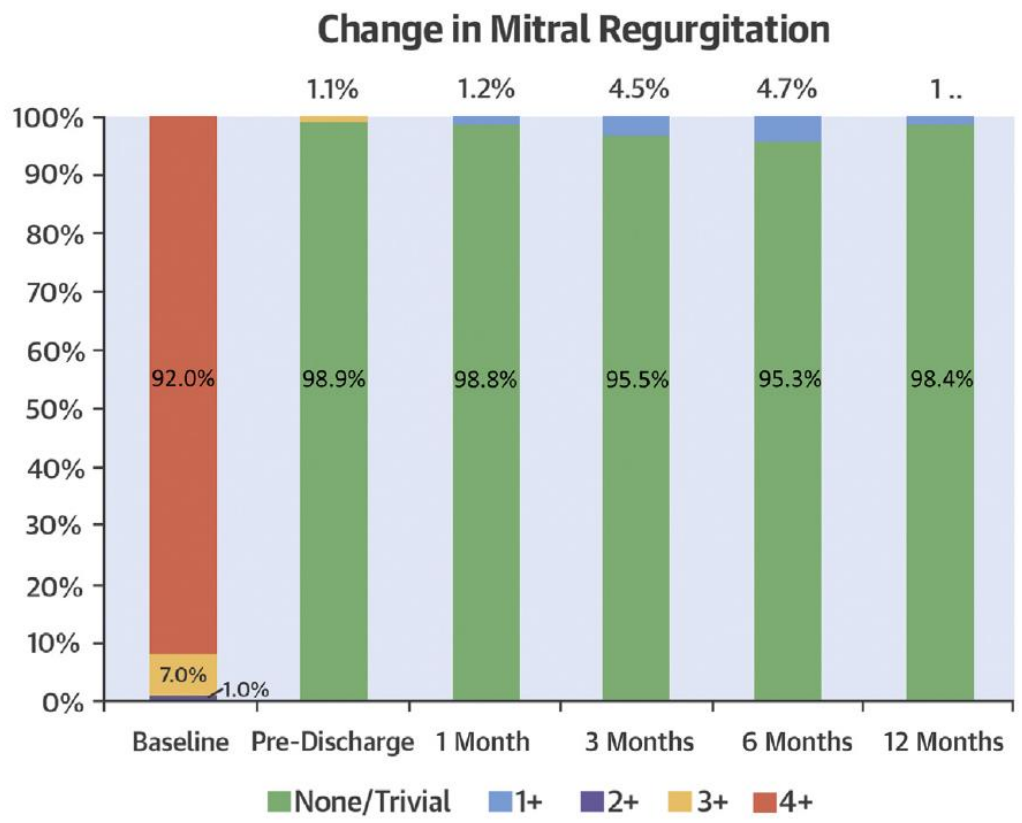
TMVR- Functional MR
Tether tightened

Tendyne Global Registry (CE)
n=100

First 100 Patients Treated

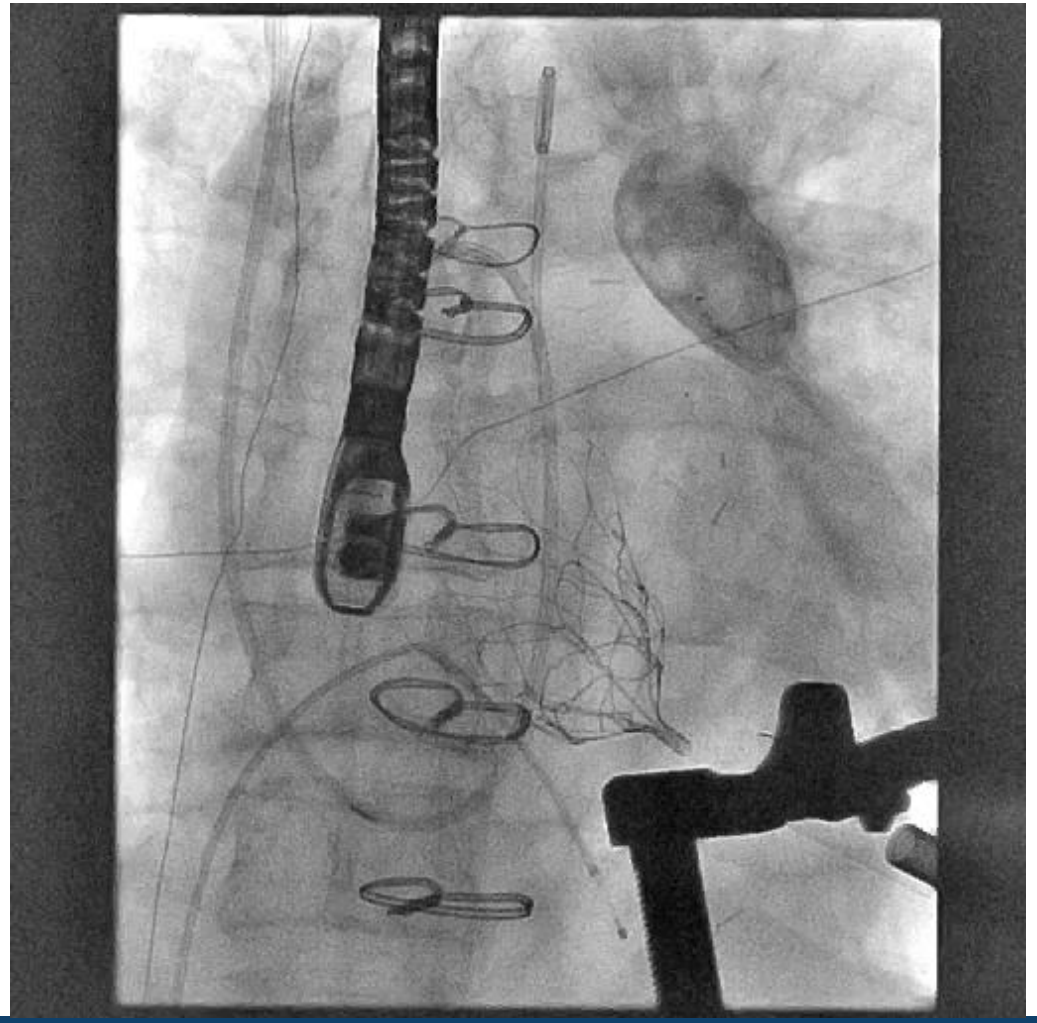


- No intra-procedural deaths
- Technical success in 96%
- 30-day death, 6%; 1-year mortality, 26%
- Among survivors at 1 year, 88.5% with mild or no symptoms



Sorajja, P. et al. J Am Coll Cardiol. 2019;73(11):1250-60.

Tendyne n=100



	30 Days	1 Year
Any mortality	6 (6)	26 (26)
Cardiovascular mortality	4 (4)	22 (22)
Disabling stroke	2 (2)	3 (3)
TIA	0 (0)	3 (3)
Myocardial infarction	2 (2)	4 (4)
Heart failure hospitalization	12 (12)	31 (31)
Reintervention for MV*	1(1)	4 (4)
BARC 2, 3, or 5 bleeding	20 (20)	32 (32)
Device-specific adverse events	4 (4)	12 (12)
Bioprosthetic valve dysfunction	0 (0)	0 (0)
Hemolysis	1 (1)	3 (3)
Embolization	0 (0)	0 (0)
Thrombosis	1 (1)	6 (6)
Erosion, migration, malposition	2 (2)	4 (4)
Fracture	0 (0)	0 (0)
Endocarditis	1 (1)	2 (2)

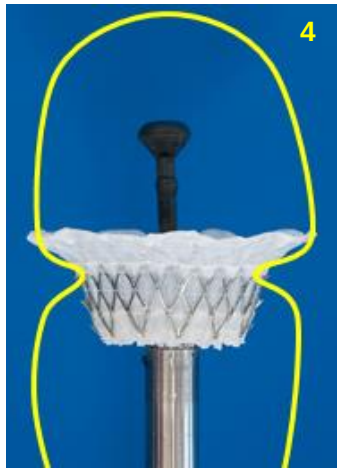
Sorajja P et al JACC 2019;73:1250.

Intrepid
Transapically implanted self-expanding valve

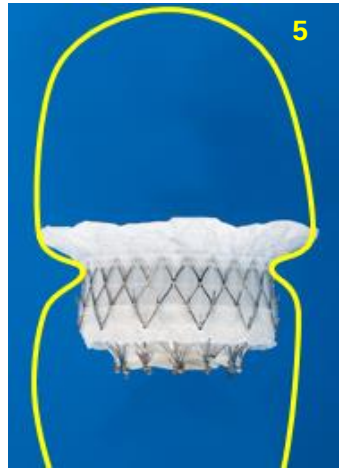
Advance across mitral valve

Deploy brim

Retract to desired position



Expand fixation ring



Release

Percutaneous Replacement- Intrepid Valve
50 patients- 72% FMR

TABLE 2 Adverse Events

	0-30 Days (n = 50)	>30 Days (n = 41)
Death	7 (14.0)	4 (9.8)
Cardiovascular	7 (14.0)	4 (9.8)
Noncardiovascular	0 (0.0)	0 (0.0)
Stroke	2 (4.0)	1 (2.4)
Disabling stroke	0 (0.0)	0 (0.0)
Nondisabling stroke	2 (4.0)	1 (2.4)
Myocardial infarction	0 (0.0)	0 (0.0)
Acute renal impairment, stage 3	5 (10.0)	0 (0.0)
Major vascular complications	0 (0.0)	0 (0.0)
Major cardiac structural complication	2 (4.0)	0 (0.0)
Major bleeding	9 (18.0)	0 (0.0)
Reoperation for any reason	5 (10.0)	1 (2.4)
Reoperation for bleeding	5 (10.0)	0 (0.0)
Reoperation for other*	0 (0.0)	1 (2.4)

Bapat V et al. JACC 2018;71:12-21.

Edwards Sapien M3 Transseptal Delivery

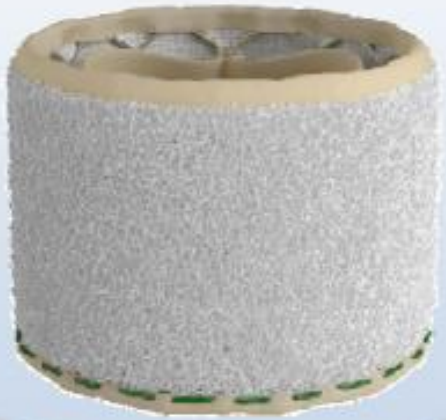
Dock Delivery

SAPIEN M3 Dock

SAPIEN M3 Dock Delivery System

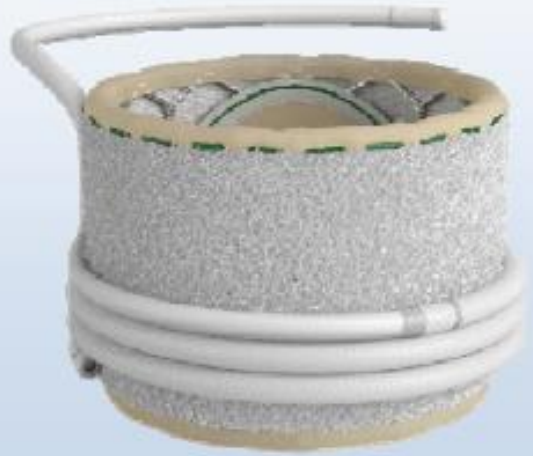
Valve Delivery

SAPIEN M3 Valve

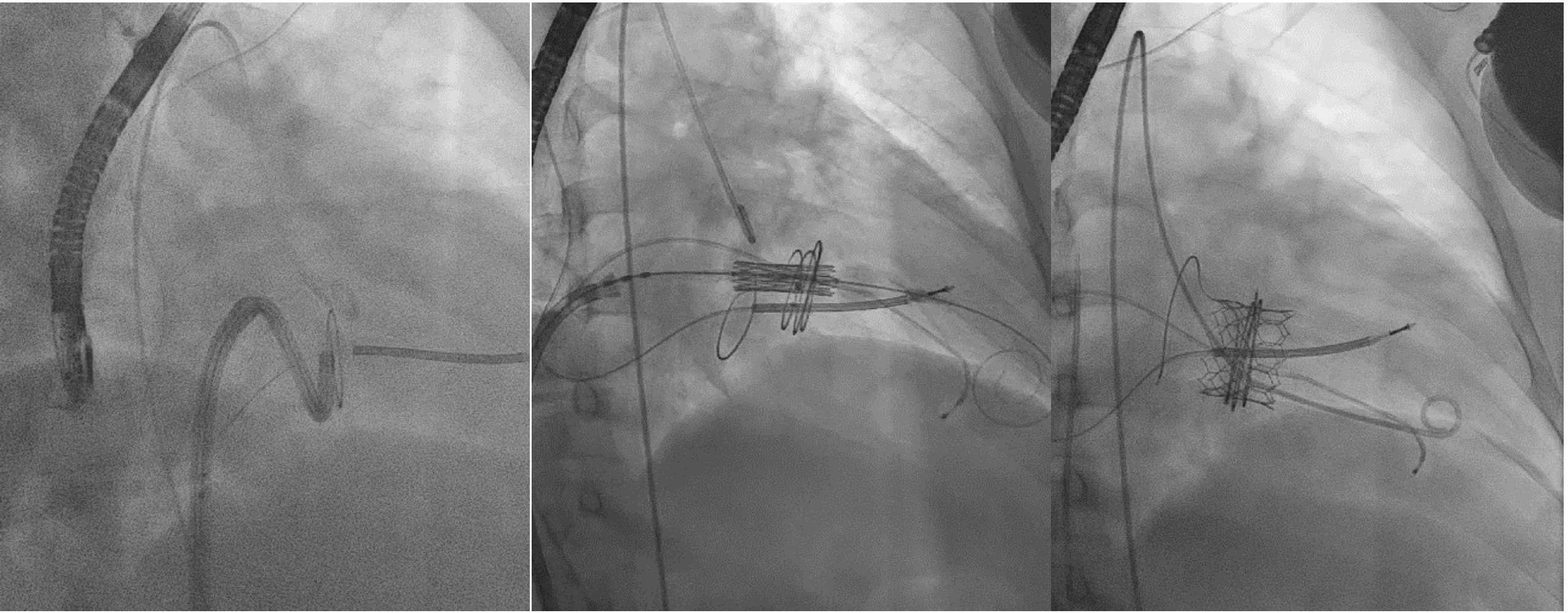


Commander Delivery System

Final Implant



M3 Docking system



M3
EFS and Canadian data

Primary Endpoint	CU (N=10) % (n/N)	EFS (N=35) % (n/N)	Total (N=45) % (n/N)
Technical Success	90 (9/10)	88.6 (31/35)	**88.9 (40/45)**
Alive	100 (10/10)	100 (35/35)	**100 (45/45)**
Successful access, delivery, and retrieval of delivery systems	90 (9/10)*	91.4 (32/35)**	**91.1 (41/45)**
Deployment of devices in intended position	90 (9/10)*	94.3 (33/35)†	**93.3 (42/45)**
Freedom from emergency surgery or reintervention related to the device or access procedure	100 (10/10)	97.1 (34/35)‡	**97.8 (44/45)**

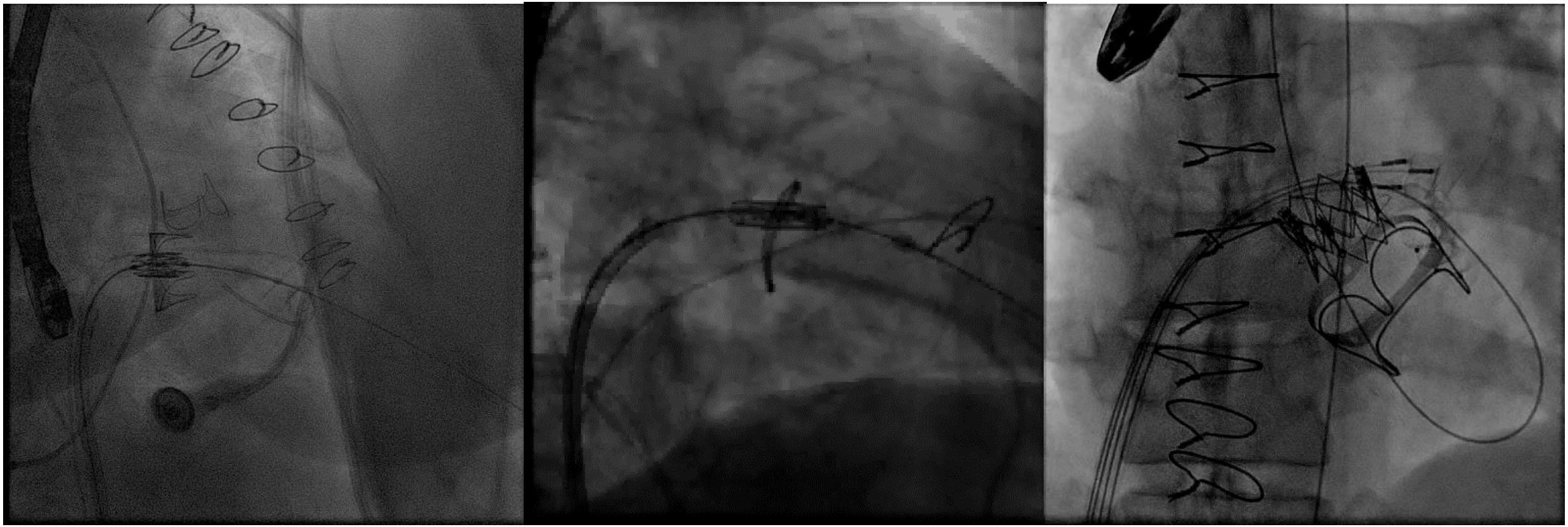
* One patient had an aortic hematoma during encircling and case was aborted

** One patient had separate transseptal punctures for deployment of the docking system and valve; one patient's left ventricle was too small to allow for encircling of chordae; one patient had an aortic hematoma during encircling and case was aborted

† Same as latter two cases above with unsuccessful delivery

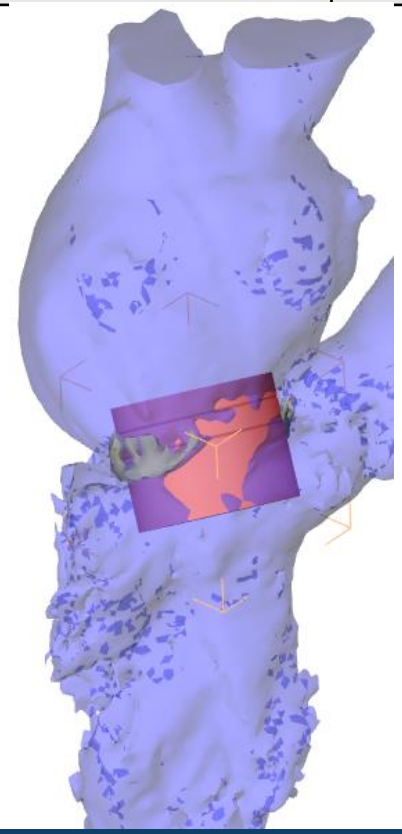
‡ One patient underwent percutaneous PVL closure during the index procedure

Post-mitral valve surgical failures
Valve-in-valve, valve-in-ring, PVL repair

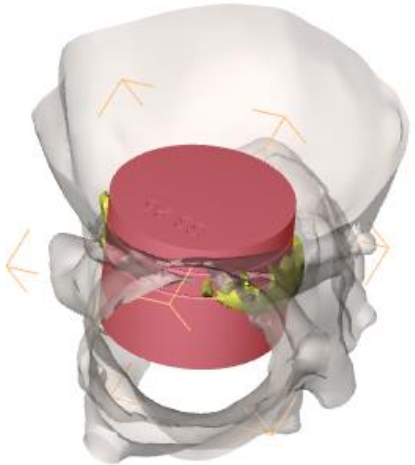


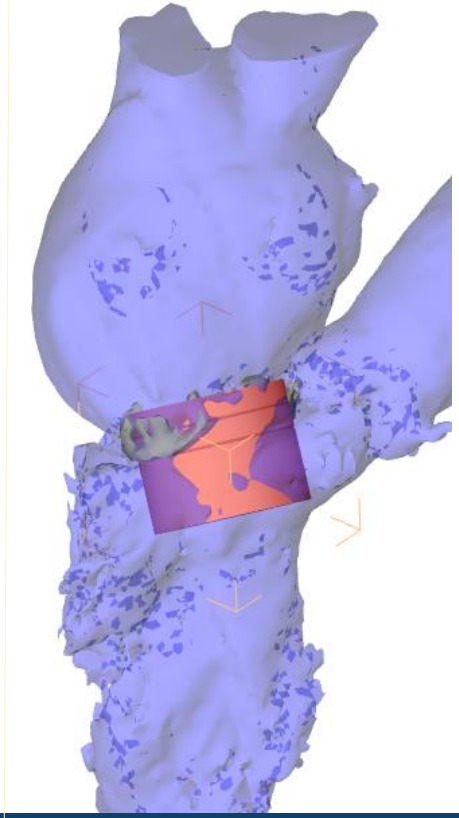
CT LVOT prediction modeling: 26 S3

Valve	Position (LV/LA)	Baseline LVOT surface area (mm^2)	Predicted Neo-LVOT surface area (mm^2)
26 S3	60/40	249.7	139.1
	80/20	234.7	65.4

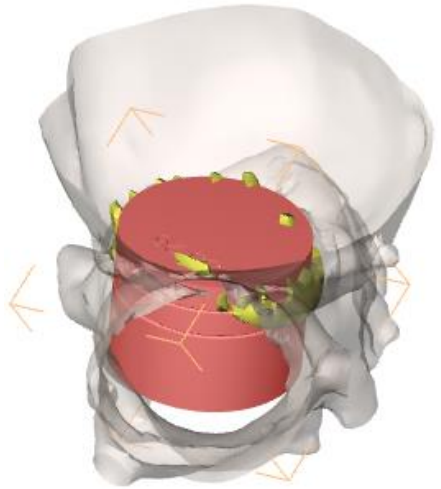


26 S3
60LV/40LA

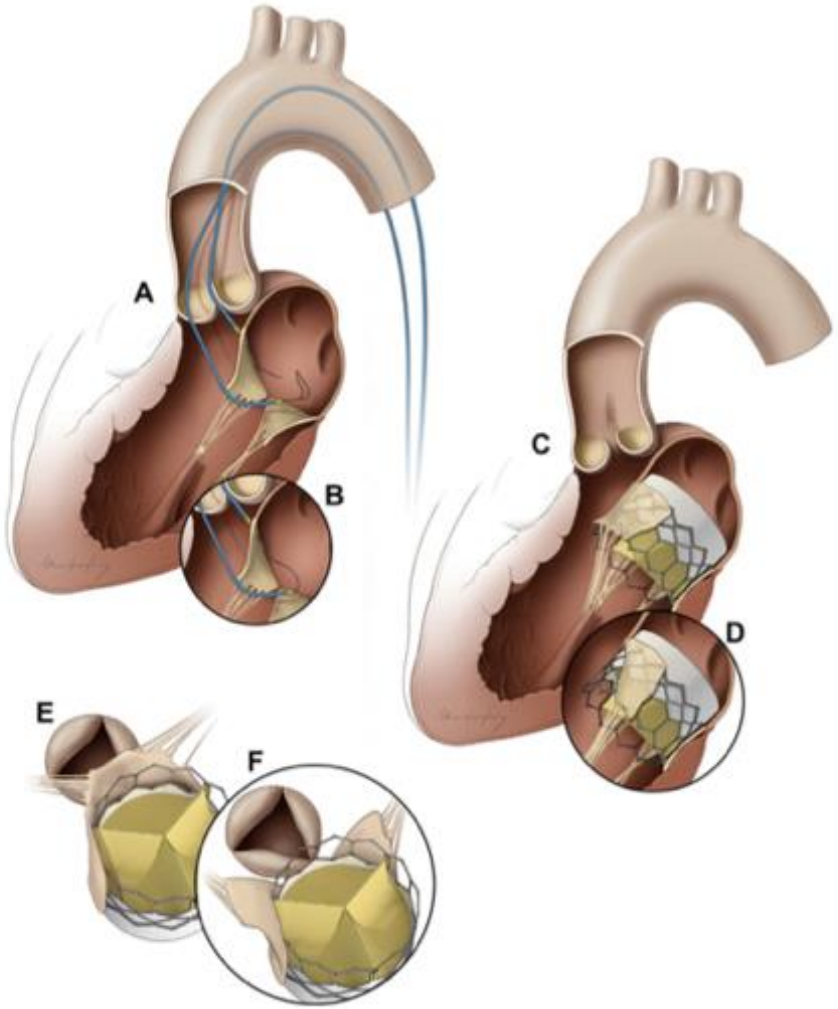


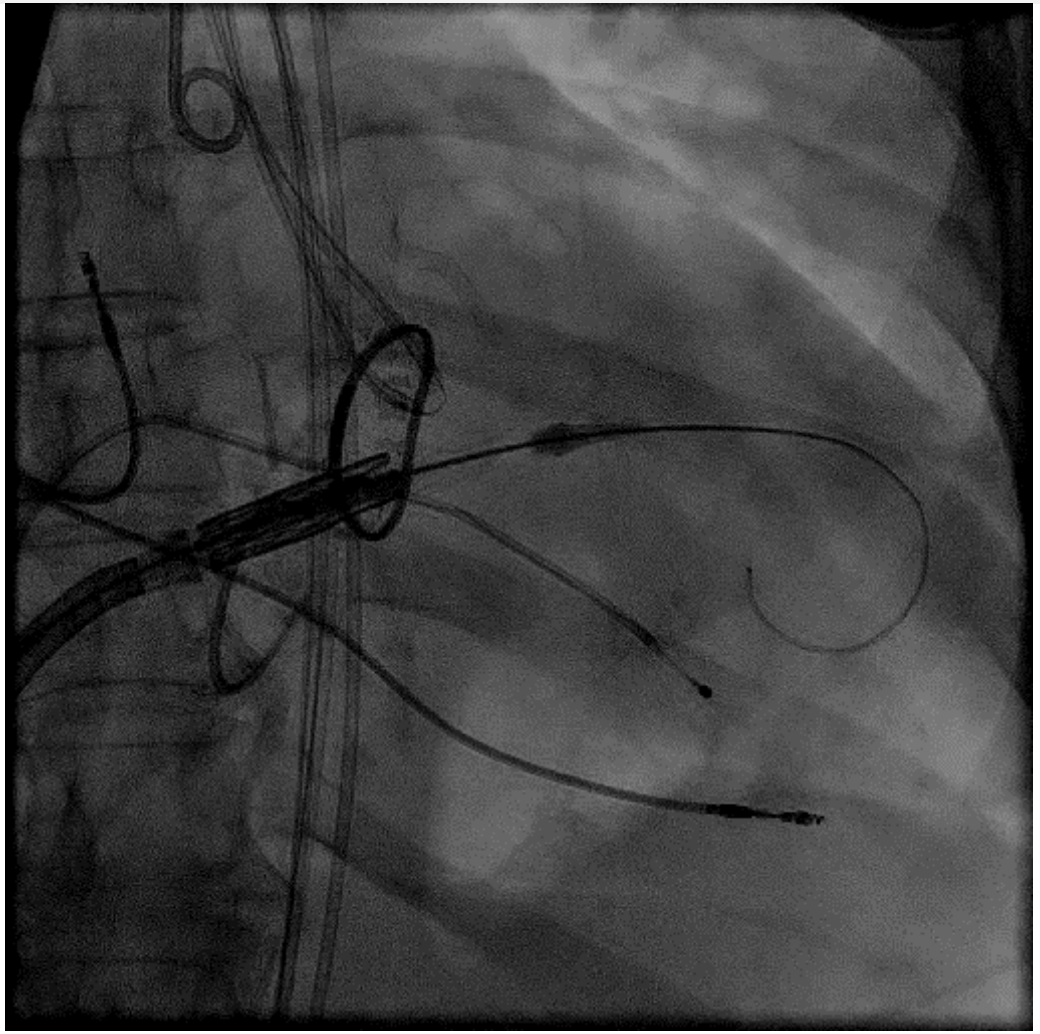


26 S3
80LV/20LA



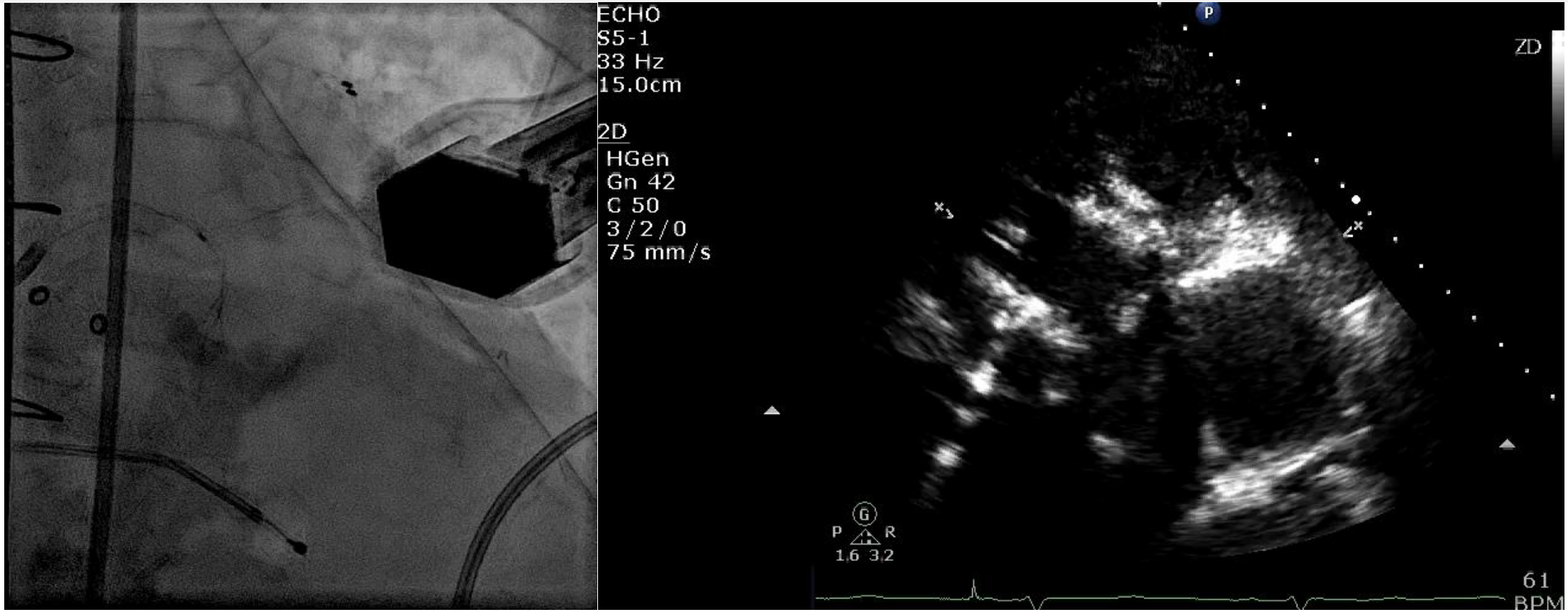
Risk of LVOT Obstruction
Intentional Laceration of the Anterior leaflet



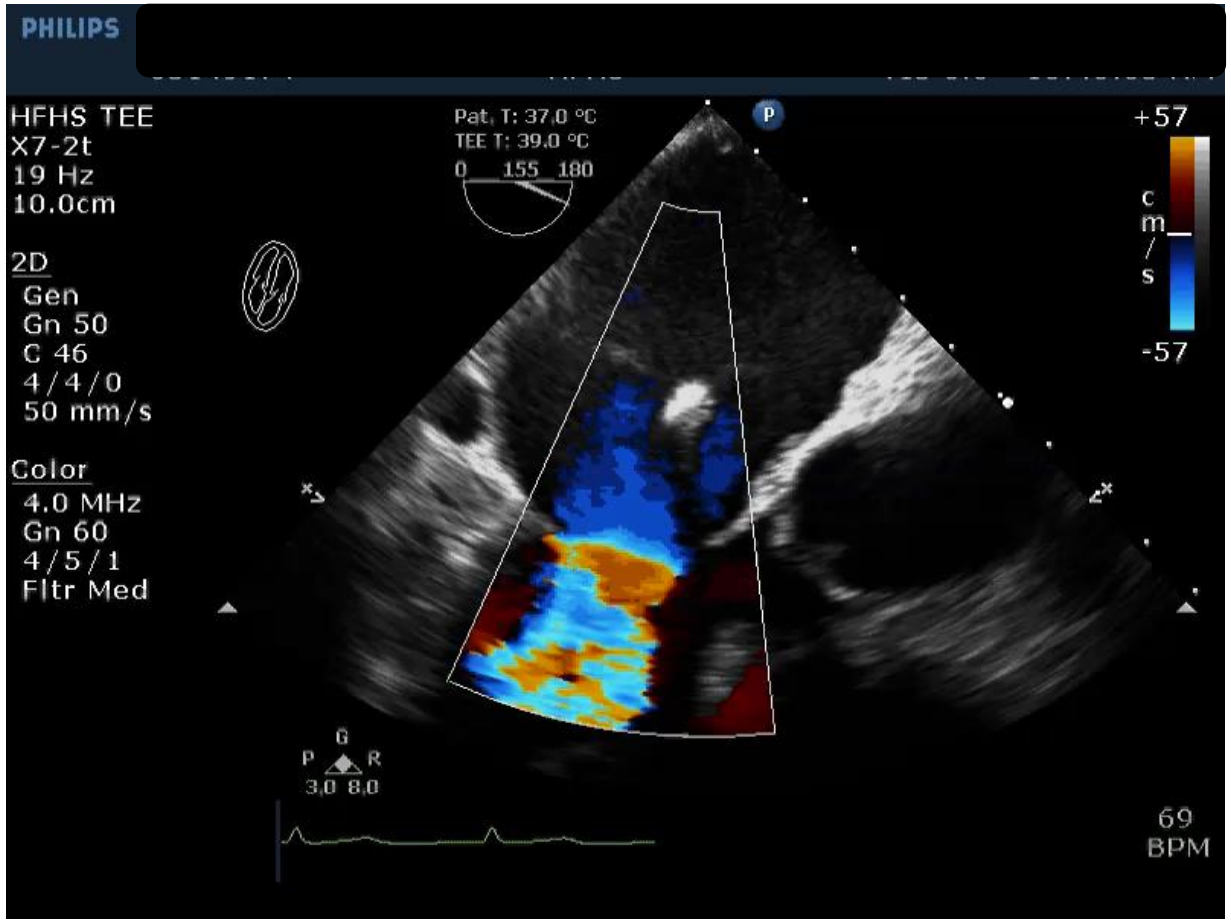


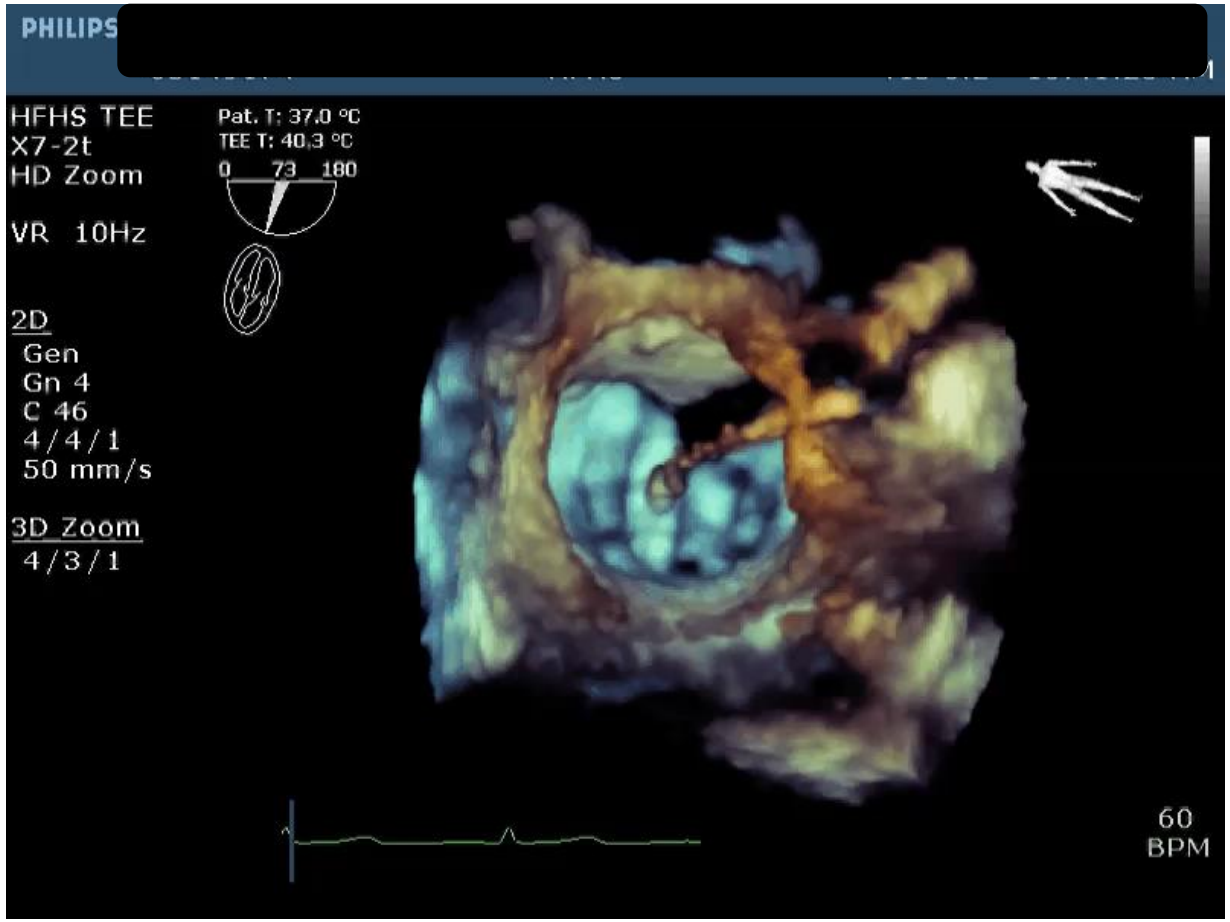
Babilarios V et al. JACC Int. 2017;10:798-809.

High-risk for LVOT obstruction
Pre-emptive alcohol septal ablation

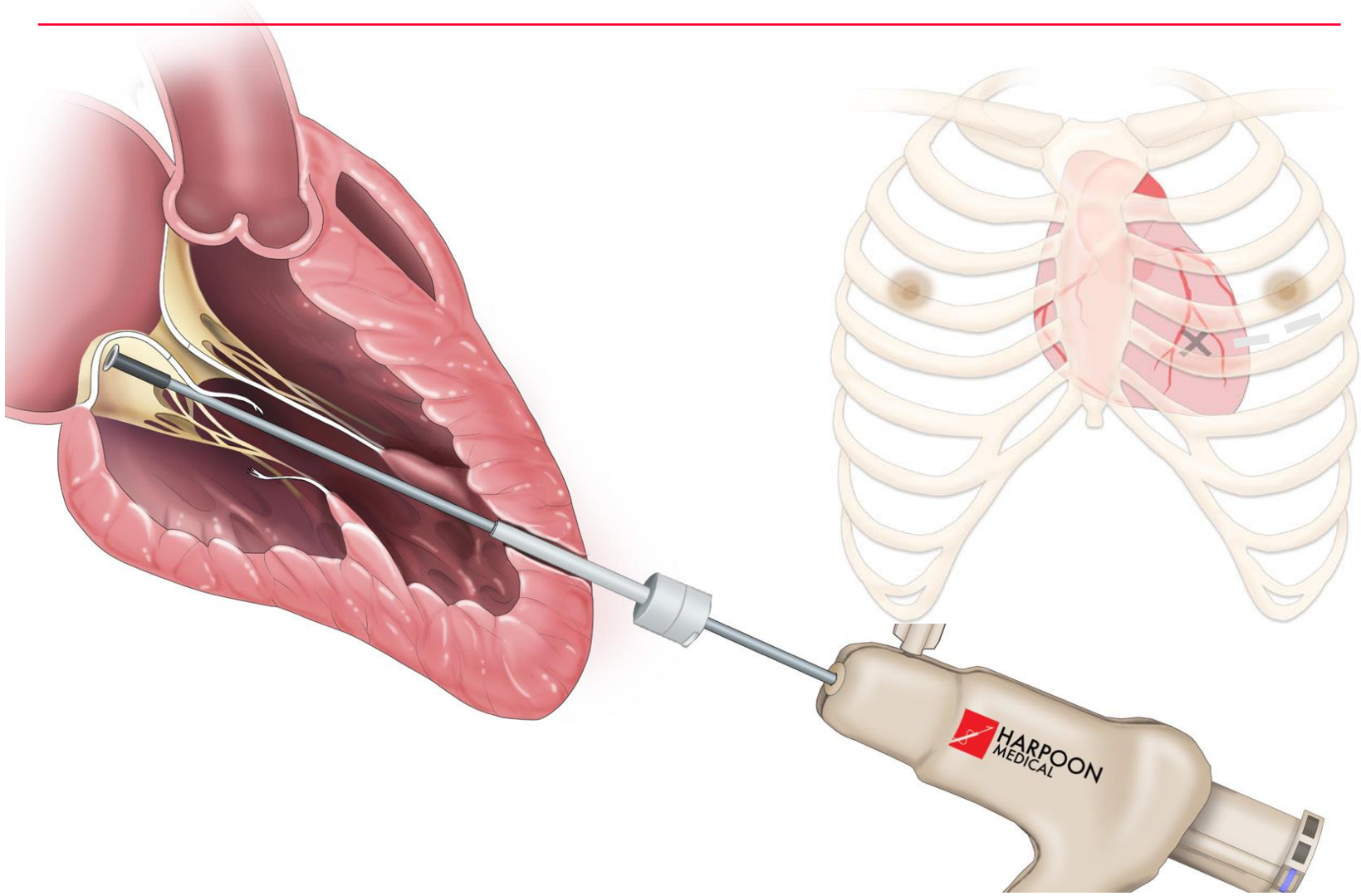


Mitra-Clip
Mitral Valve Repair



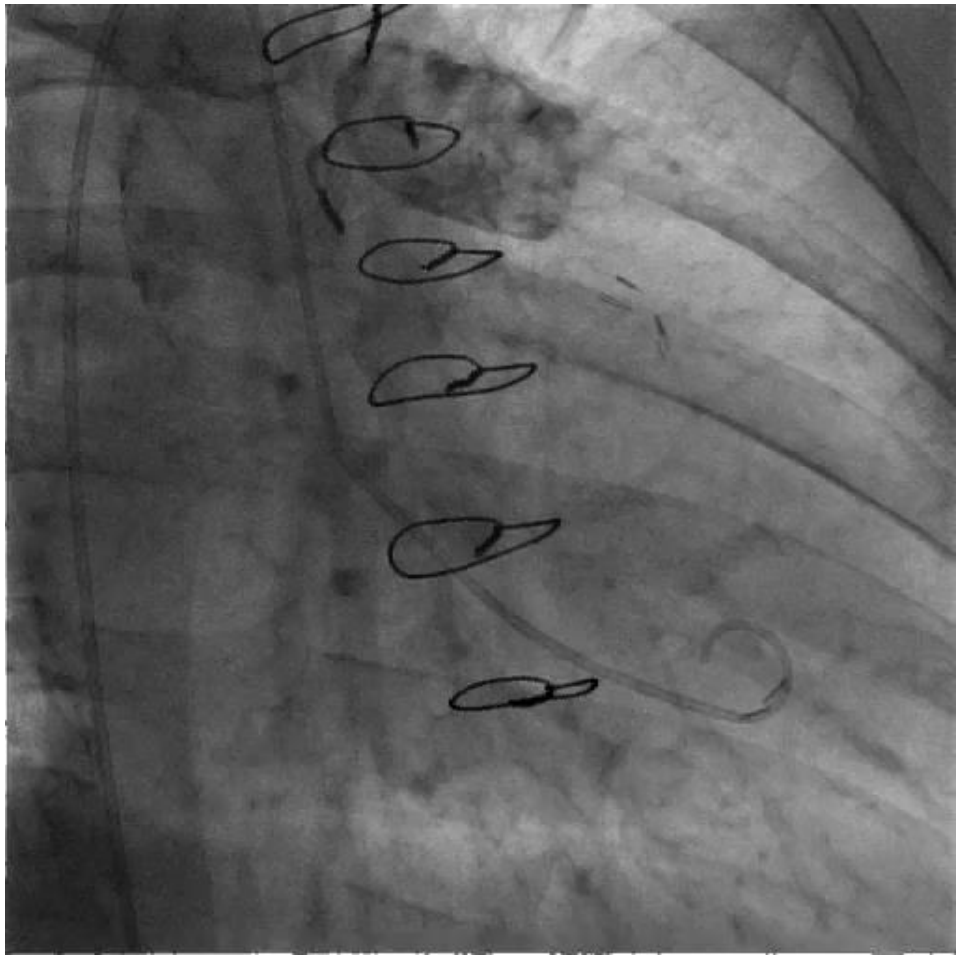


Harpoon: Fast Simple Procedure

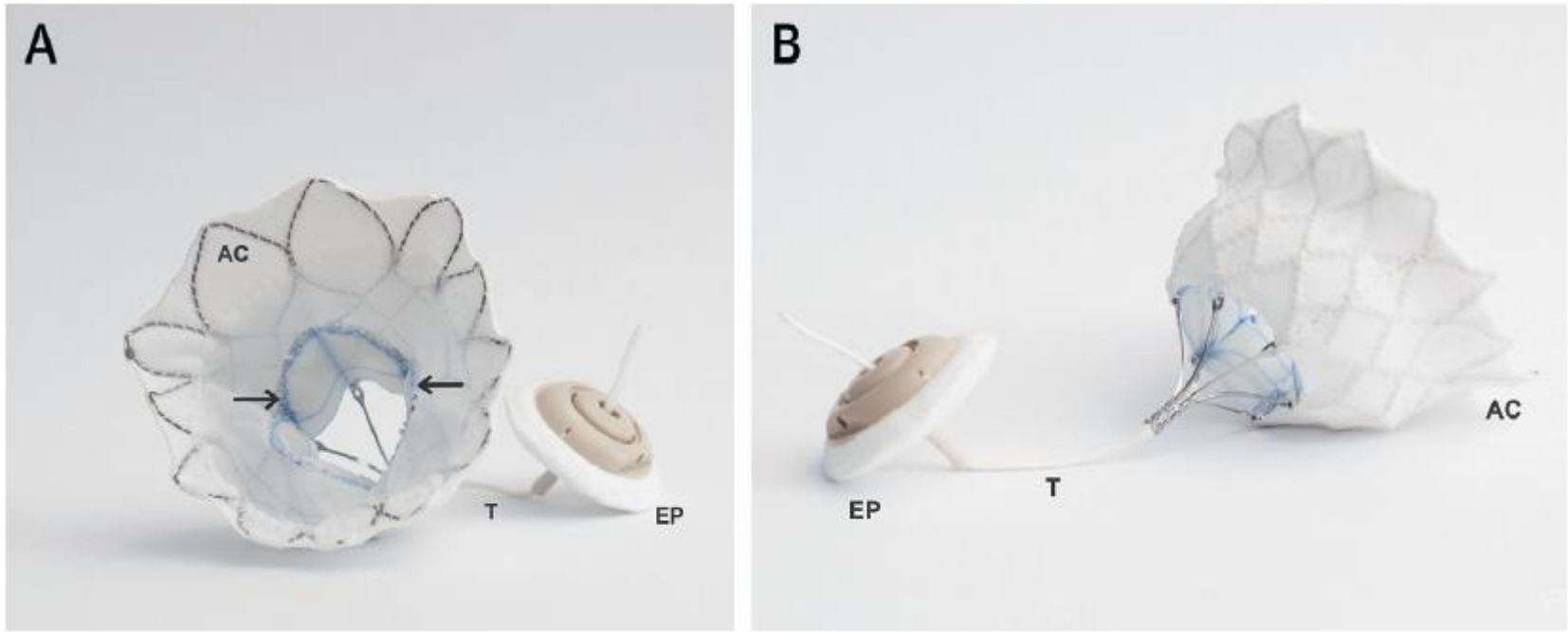


Gammie J TCT 2017

TMVR- Functional MR
Baseline Angiography



TMVR- Degenerative/Functional MR
Tendyne Prosthesis



Muller, DWM et al. JACC 2017;69:381-91.

TMVR- Functional MR
Mitral Annular Segmentation

Courtesy of J. Leipsic and P. Blanke