Saint Luke's
MID AMERICA HEART INSTITUTE

Mitral Valve Therapies for Heart Failure Patients

Adnan K. Chhatriwalla MD, FACC
Saint Luke's Mid America Heart Institute
University of Missouri - Kansas City

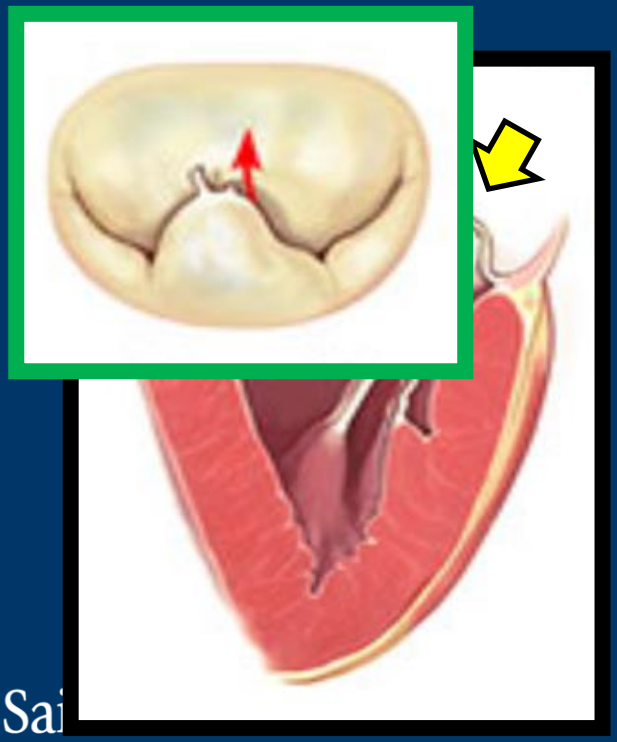
Disclosures

- Proctor: Edwards Lifesciences, Medtronic Inc.
- Speaker Bureau: Abbott Vascular, Edwards Lifesciences, Medtronic Inc.
- Consultant: Silk Road Medical

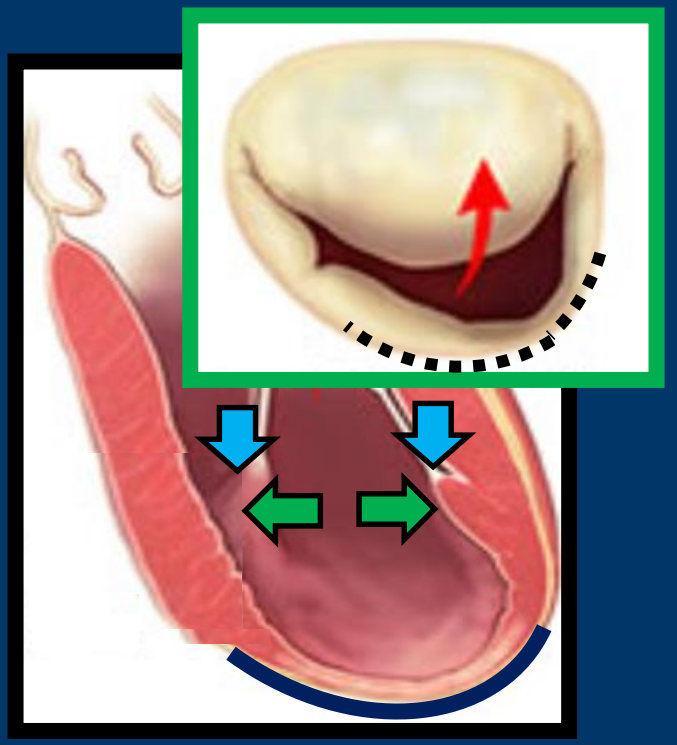
Saint Luke's
MID AMERICA HEART INSTITUTE

All MR Are Not Created Equal

For primary MR, the disease is solely a valvular lesion



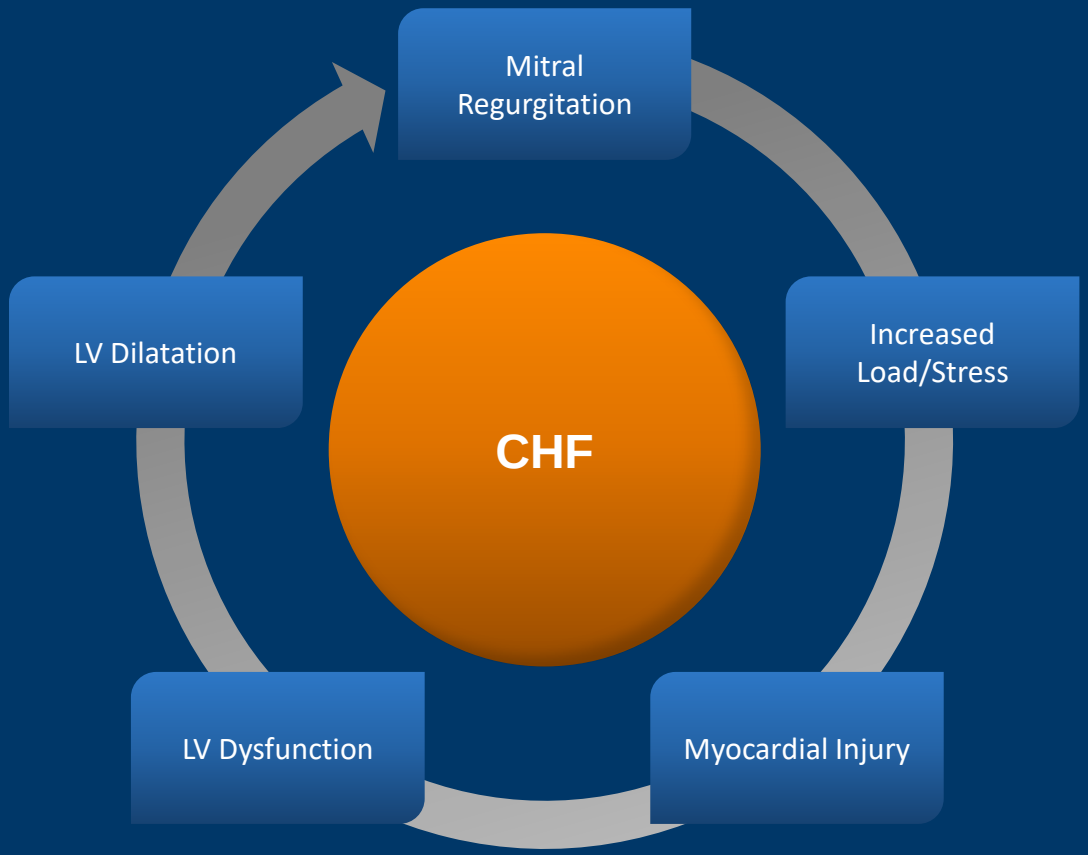
For secondary MR, LV pathology is the primary issue



MID AMERICA HEART INSTITUTE

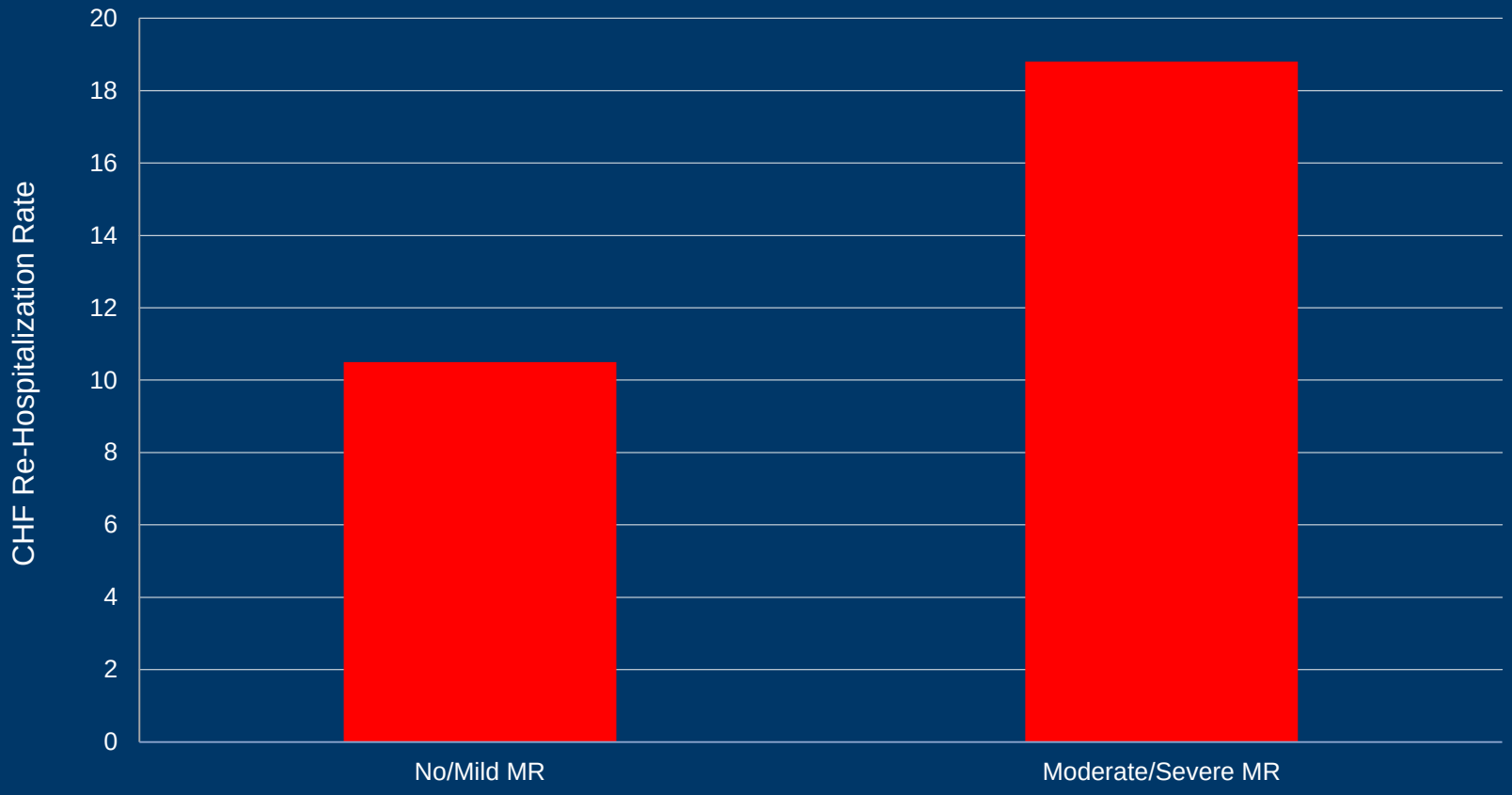
Carabello. JACC 2014;64:193-5

MR Leads to Heart Failure



Saint Luke's
MID AMERICA HEART INSTITUTE

Hospital Admissions for CHF

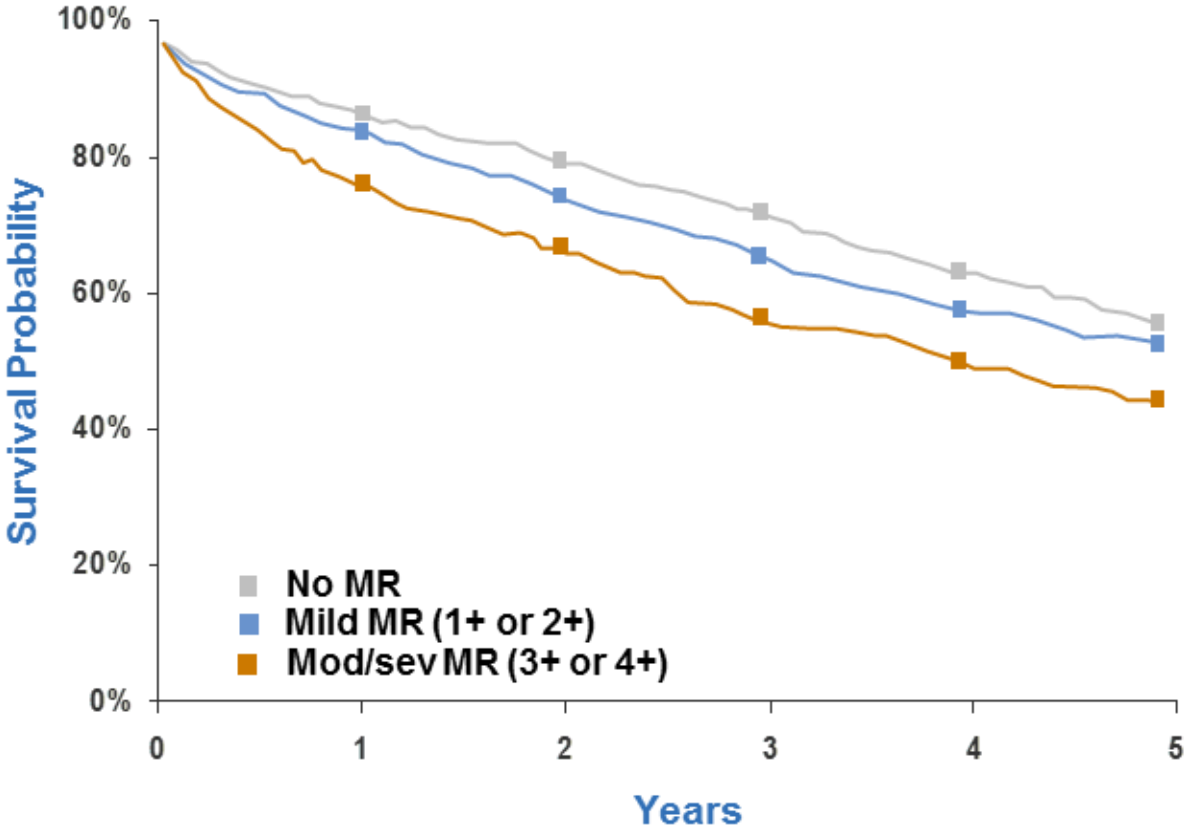


Saint Luke's
MID AMERICA HEART INSTITUTE

Markwick et al. TCT 2012

Impact of MR on Survival

Trichon BH et al. Am J Card. 2003,91:538-43



Survival of Heart Failure Patients with MR by Degree of MR
Adjusted for demographics and clinical variables at baseline

Medical Management of MR

A Randomized Controlled Phase IIb Trial

Effect of *Losartan* on Degree of Mitral

Effect of *Enalapril* Therapy on Left Ventricular Mass

Effects of angiotensin-converting enzyme inhibition on mitral regurgitation severity, left ventricular size, and

Effects of Afterload Reduction on Vena Contracta Width in Mitral Regurgitation

Saint Luke's
MID AMERICA HEART INSTITUTE

2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the American Association for Thoracic Surgery, American Society of Echocardiography, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons

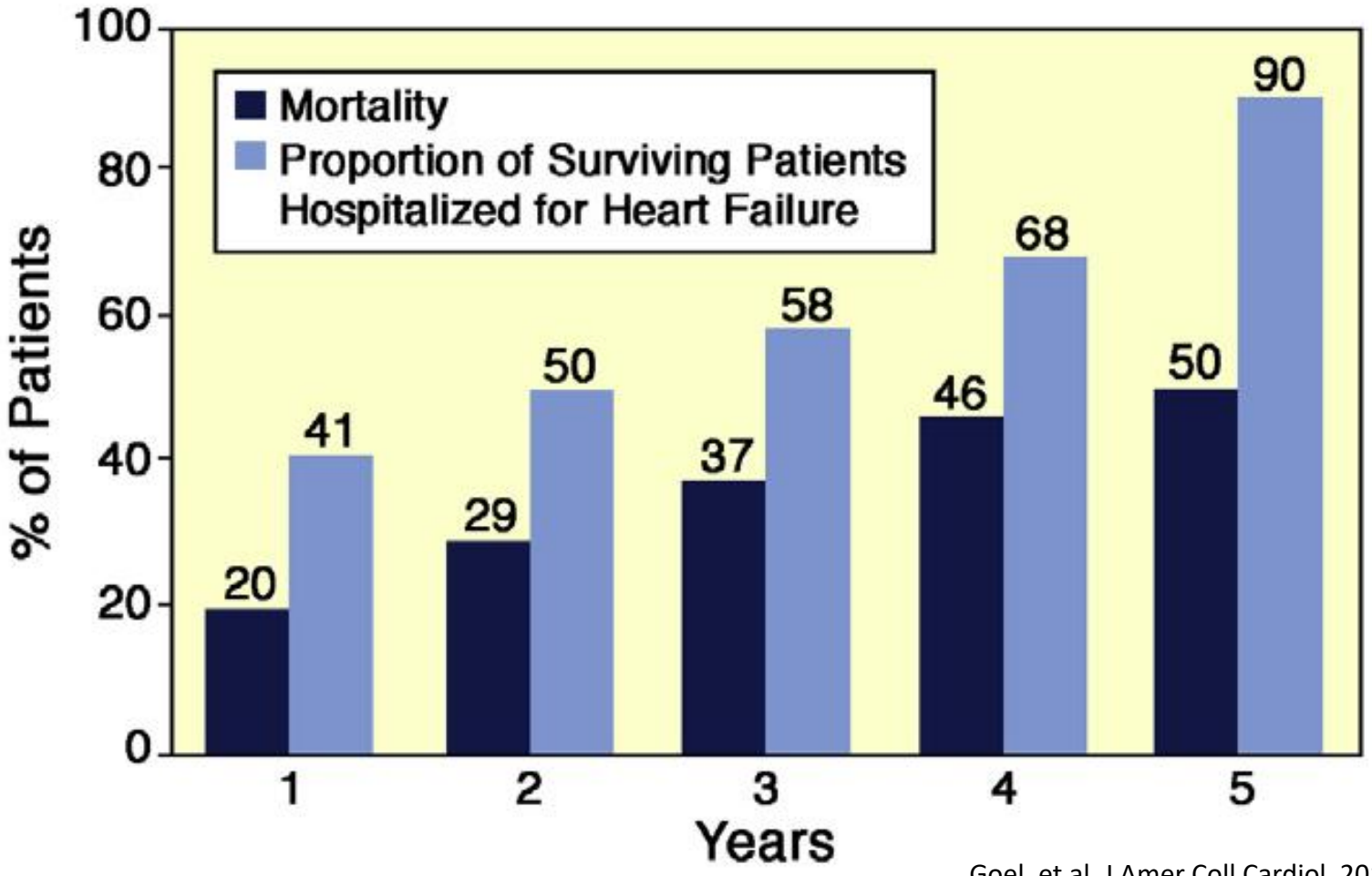
CLASS IIa

1. **Medical therapy for systolic dysfunction is reasonable in symptomatic patients with chronic primary MR (stage D) and LVEF less than 60% in whom surgery is not contemplated (382–386). *(Level of Evidence: B)***

CLASS III: No Benefit

1. **Vasodilator therapy is not indicated for normotensive asymptomatic patients with chronic primary MR (stages B and C1) and normal systolic LV function (386–391). *(Level of Evidence: B)***

Outcomes with Medical Management of MR



Goel, et al. J Amer Coll Cardiol. 2014: 185-190

Troubling Data

For asymptomatic pts with primary severe MR and EF 50-60%, only 57% of Canadian cardiologists referred these patients to surgery.[1]

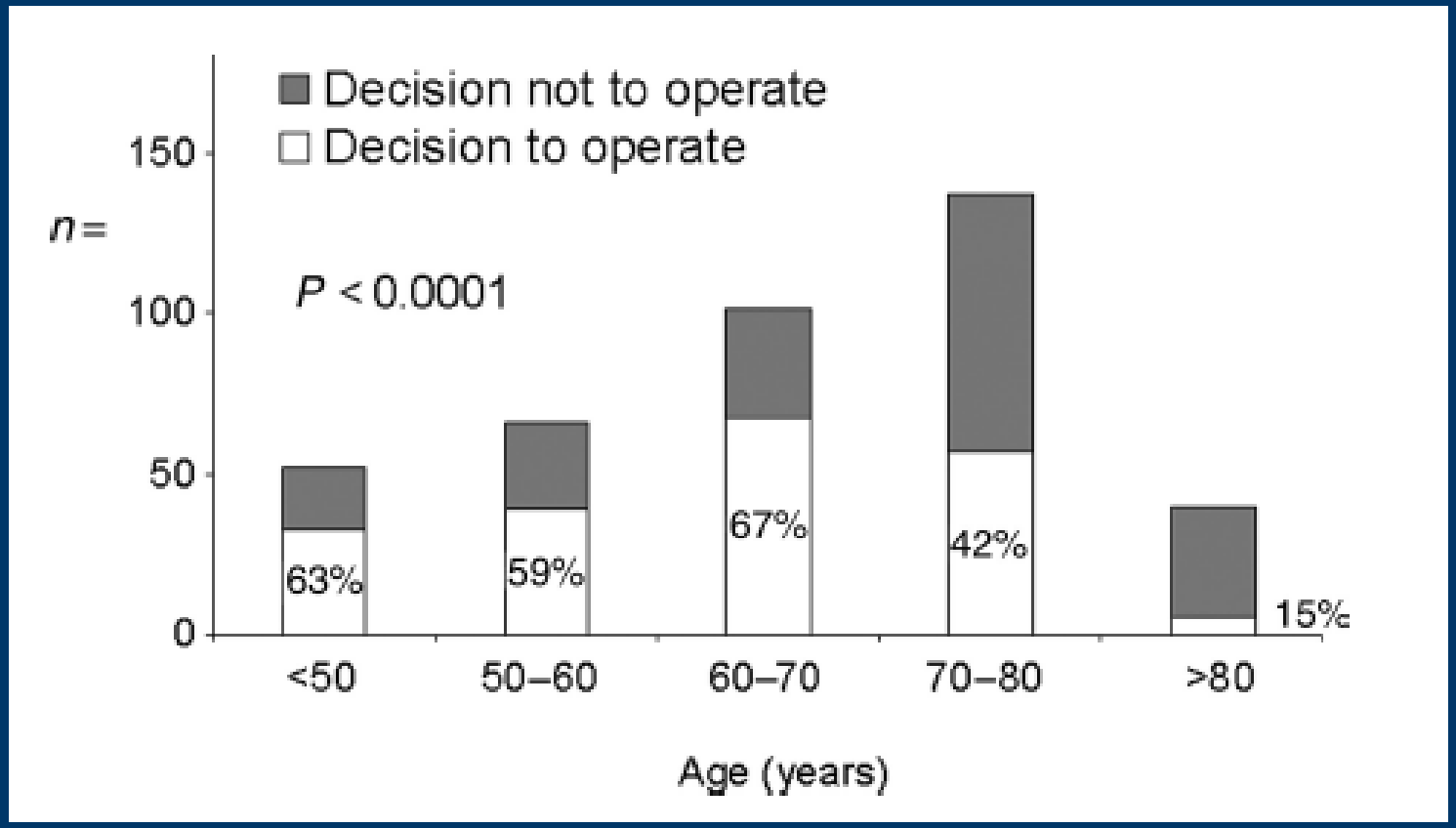
EuroHeart survey, 49% of symptomatic pts with severe MR did not receive a surgical evaluation.[2]

Univ of Michigan, ½ of the 112 pts with severe primary MR underwent surgery. Of those who did not have surgery, 75% had $\geq$ 1 indication.[3]

Saint Luke's
MID AMERICA HEART INSTITUTE

[1] Can J Cardiol 2007;23:209-14. [2] Eur Heart J. 2007;28:1358-65 [3]JACC 2009;54:860-5

Surgery is Underutilized



Saint Luke's
MID AMERICA HEART INSTITUTE

Mirabel et al. *Eur Heart J* 2007; 28: 1358-1365.

What Are Our Options?

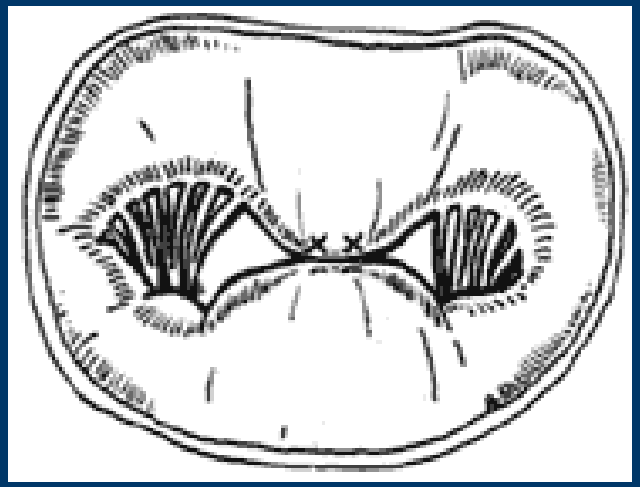
"Your medical problems are more complicated than I thought. I am going to refer you to another doctor, who has more medical insurance than I have."

Need for Alternative Therapies

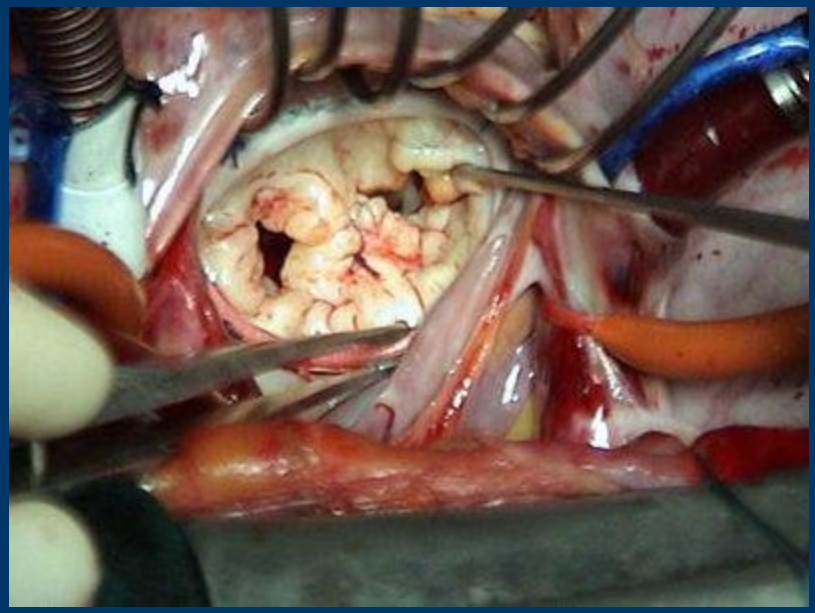
- Evolving technologies are all based upon surgical techniques
  - Edge-to-Edge Repair (Alfieri technique)
  - Annuloplasty
    - Indirect
    - Direct
  - Chordal Replacement
  - Percutaneous Mitral Valve Implant

Edge-to-Edge Repair: Alfieri Technique

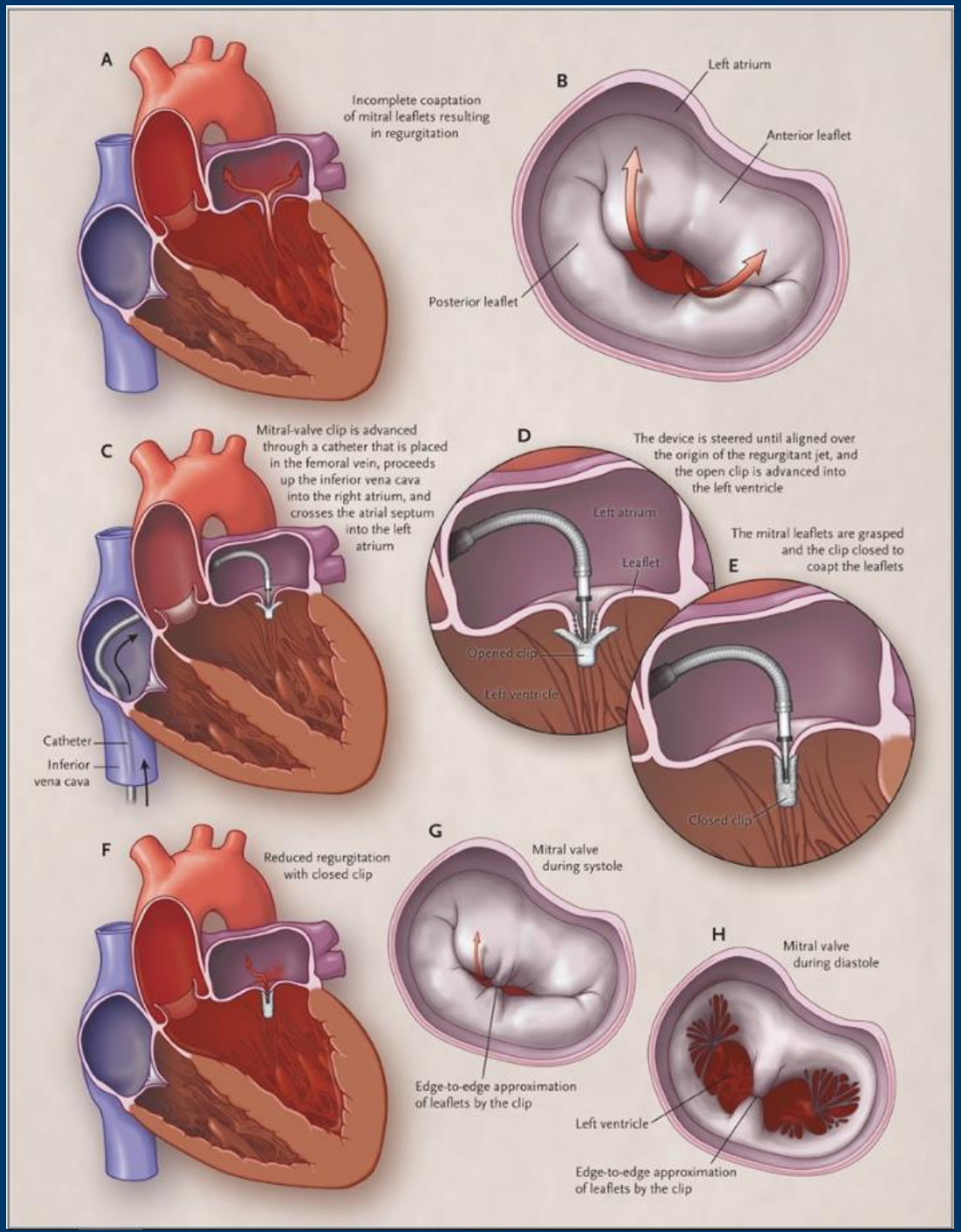
- Described in 1992
  - Suture part of anterior and posterior leaflet edges together
  - Usually applied to A2-P2 central segment



- Usually used in conjunction with mitral annuloplasty



Saint Luke's
MID AMERICA HEART INSTITUTE



The MitraClip System

EVEREST II RCT: Efficacy Results

Event	MitraClip	Surgery	p-value
Composite Efficacy Endpoint	***100 (55%)***	***65 (73%)***	***0.007***
Death	11 (6%)	5 (6%)	1.00
Surgery for MV dysfunction	*37 (20%)*	*2 (2%)*	*< 0.001*
Grade 3+ or 4+ MR	38 (21%)	18 (20%)	1.00

Saint Luke's MID AMERICA HEART INSTITUTE

N Engl J Med 2011; 364:1395-1406
DOI: 10.1056/NEJMoa1009355

EVEREST II RCT: Safety Results

Event	MitraClip	Surgery	p-value
Any Major Adverse Event	*27 (15%)*	*45 (48%)*	*< 0.001*
- *Excluding transfusion*	*9 (5%)*	*9 (10%)*	*0.23*
Transfusion ≥ 2U PRBC	24 (13%)	42 (45%)	< 0.001
Urgent CT surgery	4 (2%)	4 (4%)	0.57
Renal failure	1 (< 1%)	0	1.00
Stroke	2 (1%)	2 (2%)	0.89
Mechanical ventilation ≥ 48 hrs	0 (0%)	4 (4%)	0.02

Saint Luke's MID AMERICA HEART INSTITUTE

N Engl J Med 2011; 364:1395-1406
DOI: 10.1056/NEJMoa1009355

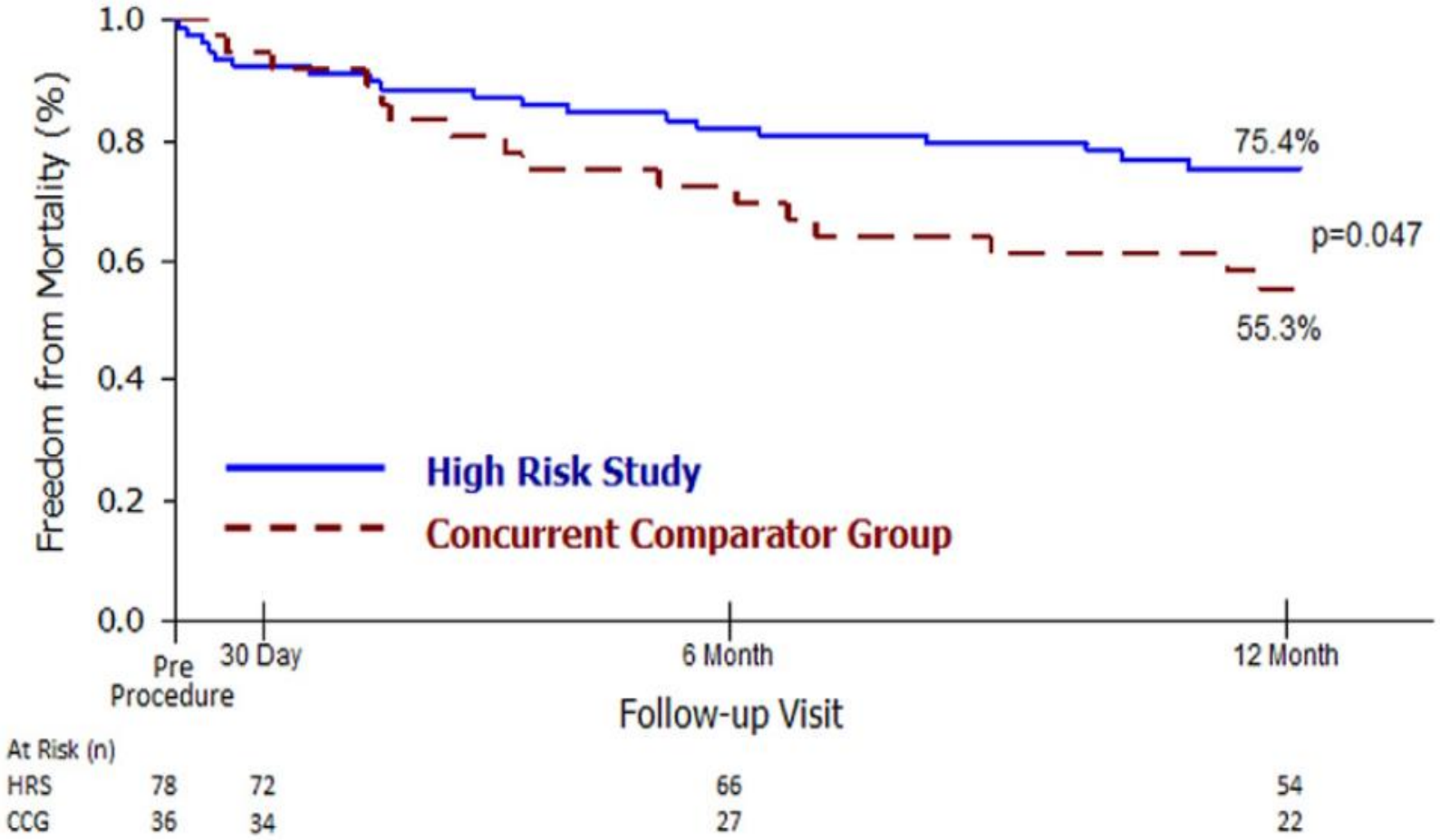
EVEREST II: Secondary Endpoints

Characteristic	MitraClip (N=184)	Surgery (N=95)	p-value
Change in LVEF	-2.8 ± 7.2 *	-6.8 ± 10.1 *	0.005
Change in EDV	-25.3 ± 28.3 *	-40.2 ± 35.9 *	0.004
Change in QOL score			
12 mo. (physical)	4.4 ± 9.8 *	4.4 ± 10.4 *	0.98
12 mo. (mental)	5.7 ± 9.6 *	3.8 ± 10.3 *	0.24
Severity of MR			< 0.001
0-1+	66 (43%)	52 (76%)	
2+	59 (39%)	14 (20%)	
3+	21 (14%)	3 (4%)	
4+	7 (5%)	0 (0%)	

Saint Luke's MID AMERICA HEART INSTITUTE

* - p value < 0.01 from baseline

EVEREST II High Risk Registry



https://doi.org/10.1016/j.jacc.2013.12.062

Current Status of the MitraClip

- October 24, 2013: FDA approved the MitraClip for the following commercial indication:
  - "*The MitraClip is intended to treat patients with significant symptomatic* ***degenerative*** *mitral regurgitation with MR ≥ 3+ who have too high a risk for surgery*"

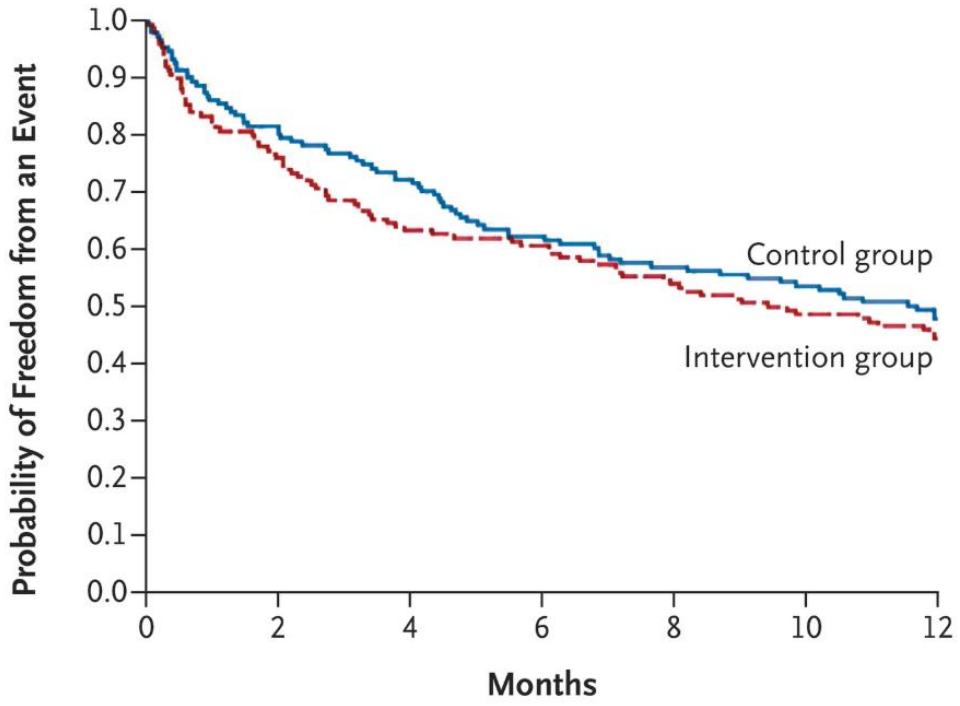
Saint Luke's
MID AMERICA HEART INSTITUTE

What about Functional MR?

ORIGINAL ARTICLE

Percutaneous Repair or Medical Treatment for Secondary Mitral Regurgitation

Jean-François Obadia, M.D., Ph.D., David Messika-Zeitoun, M.D., Ph.D., Guillaume Leurent, M.D., Bernard Iung, M.D., Guillaume Bonnet, M.D., Nicolas Piriou, M.D., Thierry Lefèvre, M.D., Christophe Piot, M.D., Ph.D., Frédéric Rouleau, M.D., Didier Carrié, M.D., Ph.D., Mohammed Nejjari, M.D., Patrick Ohlmann, M.D., et al., for the MITRA-FR Investigators.*



No. at Risk

Control group	152	123	109	94	86	80	73
Intervention group	151	114	95	91	81	73	67

Caveats:

- Only moderate MR was required for enrollment
- Majority of MC patients had ≥ 2+ MR at 12 months
- Optimal medical therapy was not mandated
- Small sample size

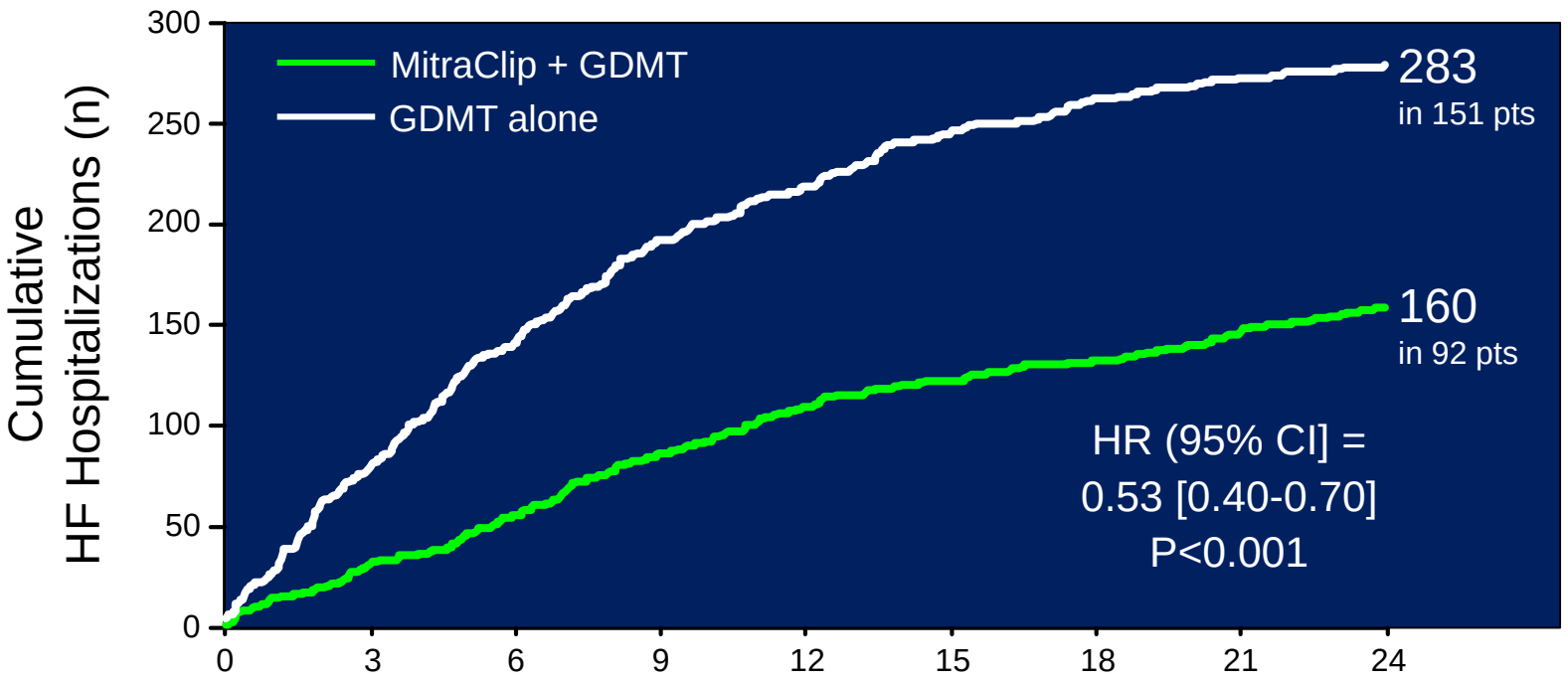
COAPT Trial

- **Design:** Prospective, multicenter, RCT
- **Objective:**
  - examine safety and efficacy of MitraClip device used in addition to standard care for *functional* MR and CHF compared to standard care alone
- **Primary Endpoints**
  - *Efficacy*: recurrent HF hospitalizations at 12 months
  - *Safety*: composite of mortality, stroke, LVAD, heart transplant or worsening kidney function at 12 months

Saint Luke's
MID AMERICA HEART INSTITUTE

COAPT Trial

All Hospitalizations for HF within 24 months



No. at Risk:									
MitraClip	302	286	269	253	236	191	178	161	124
GDMT	312	294	271	245	219	176	145	121	88

Saint Luke's
MID AMERICA HEART INSTITUTE

COAPT Trial
Powered Secondary Endpoints

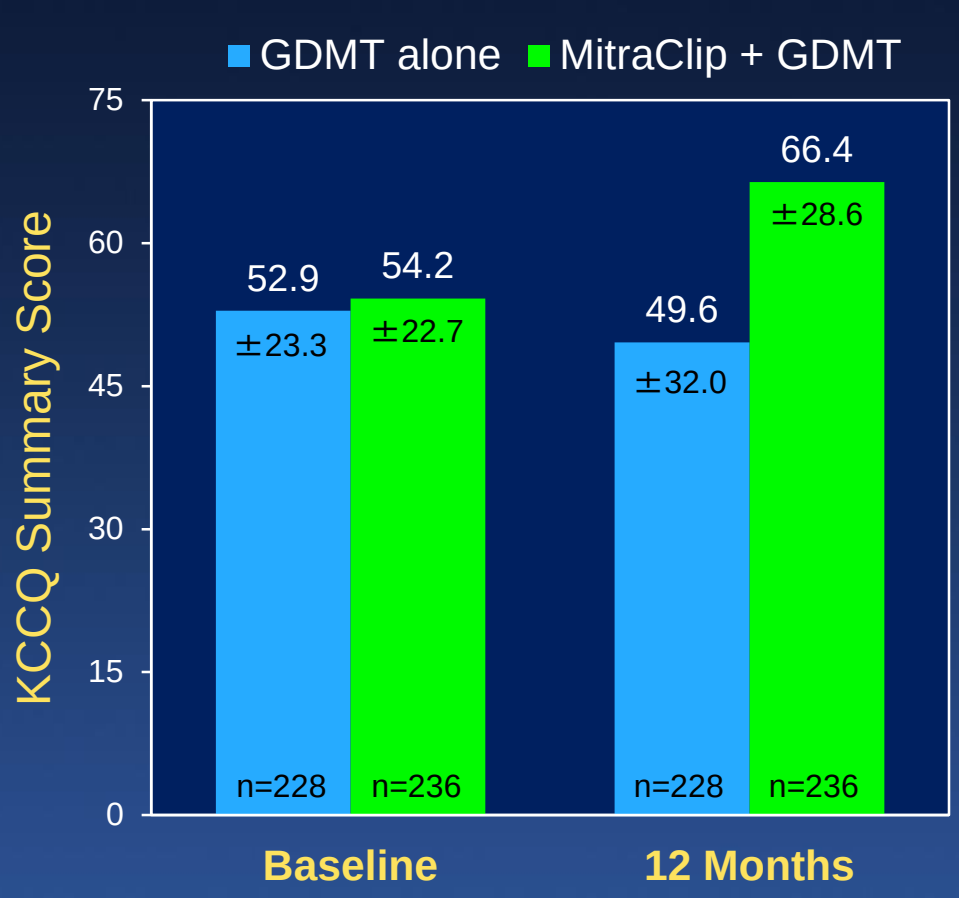
- Tested in hierarchical order[1] -

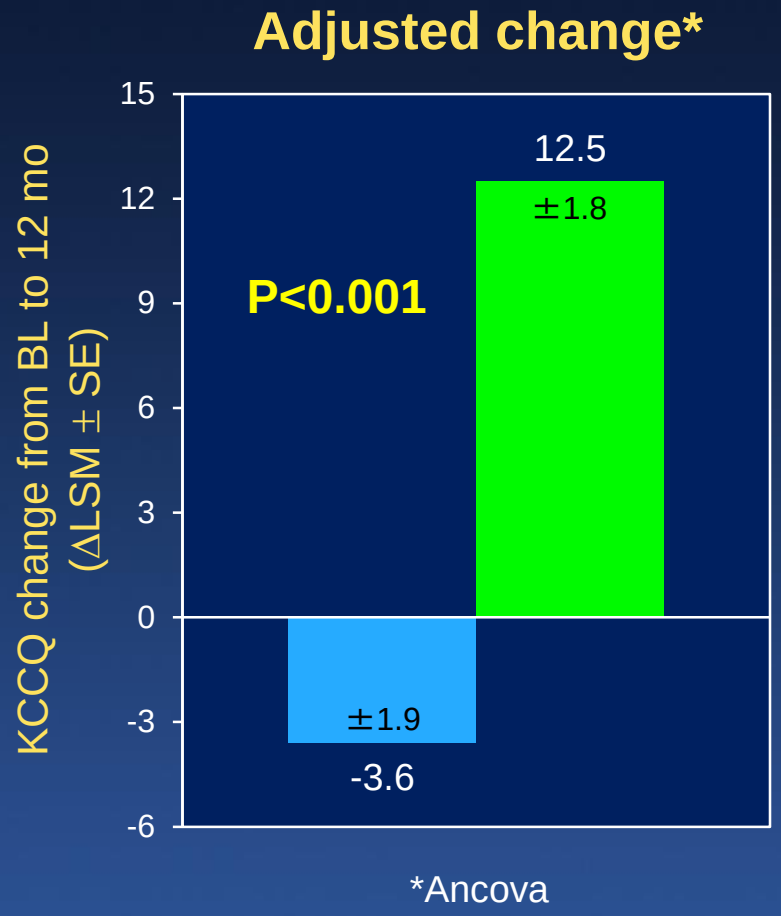
	P-value
1. MR grade ≤2+ at 12 months	<0.001
2. All-cause mortality at 12 months[2]	<0.001
3. Death and all HF hospitalization through 24 months (Finkelstein-Schoenfeld)	<0.001
4. Change in QOL (KCCQ) from baseline to 12 months	<0.001
5. Change in 6MWD from baseline to 12 months	<0.001
6. All-cause hospitalizations 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

Saint Luke's MID AMERICA HEART INSTITUTE

[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

Change in KCCQ from Baseline to 12 Months





Current Status of the MitraClip

- October 24, 2013: FDA approved the MitraClip for the following commercial indication:
  - "*The MitraClip is intended to treat patients with significant symptomatic **degenerative** mitral regurgitation with MR ≥ 3+ who have too high a risk for surgery*"
- March 14, 2019: FDA approved Mitraclip for FMR:
  - *"The Mitraclip System, when used with maximally tolerated guideline-directed medical therapy, is indicated for the treatment of symptomatic moderate-to-severe **secondary (or functional)** mitral regurgitation*

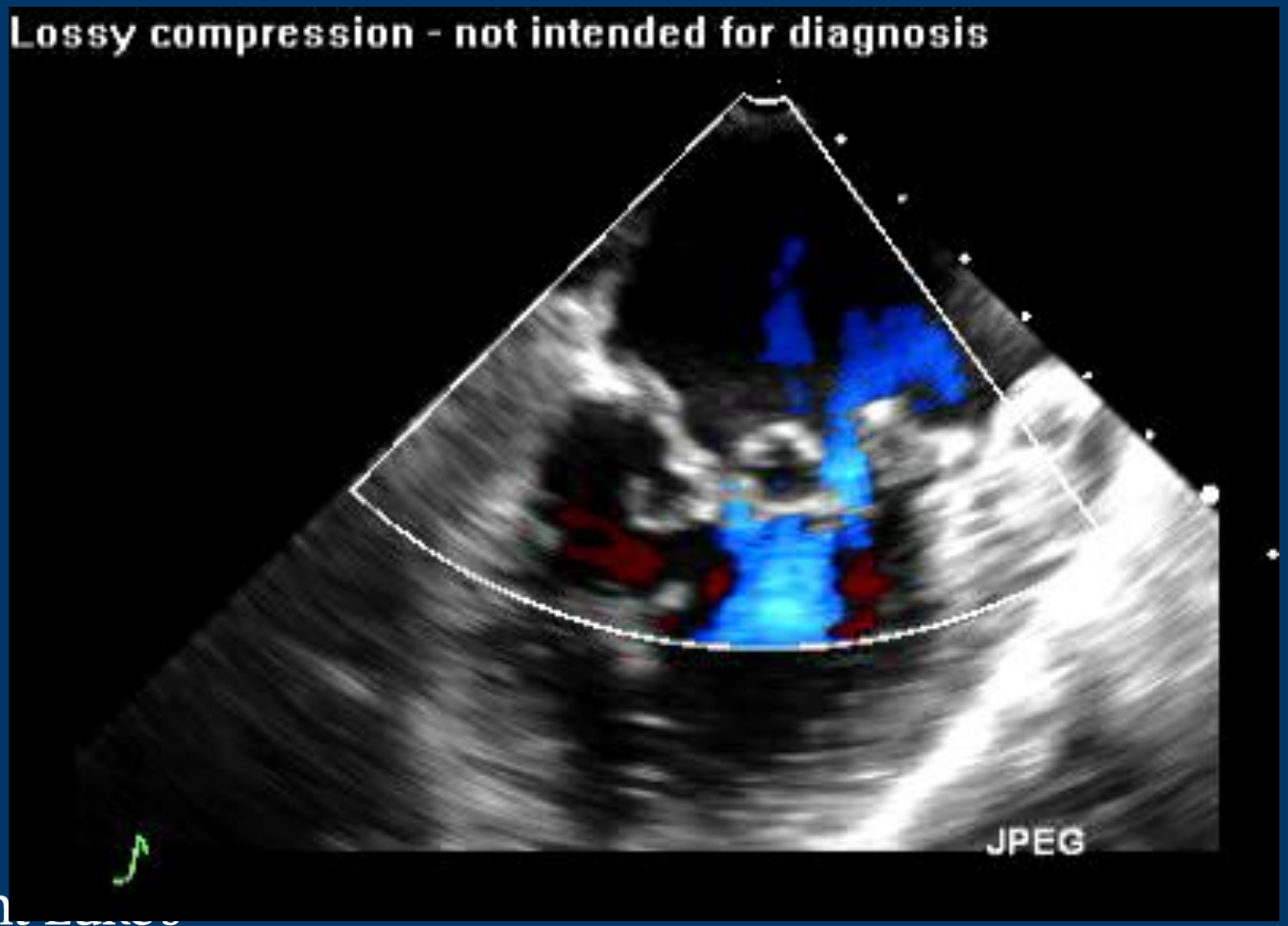
Saint Luke's
MID AMERICA HEART INSTITUTE

Case Presentation

- 89 y/o female, known severe mitral regurgitation
- *Chief Complaint*: increasing fatigue, dyspnea on exertion, weakness
- *Hx:* CKD, Hx Breast Cancer 2003 s/p lumpectomy, right nephrectomy 1970, osteoporosis
- TEE: Diffusely myxomatous mitral valve with bileaflet prolapse. Severe mitral regurgitation. Regurgitant fraction is 50%.
- Dr. Borkon: Patient is at prohibitive risk for mitral valve surgery

Saint Luke's
MID AMERICA HEART INSTITUTE

Pre-procedure TEE

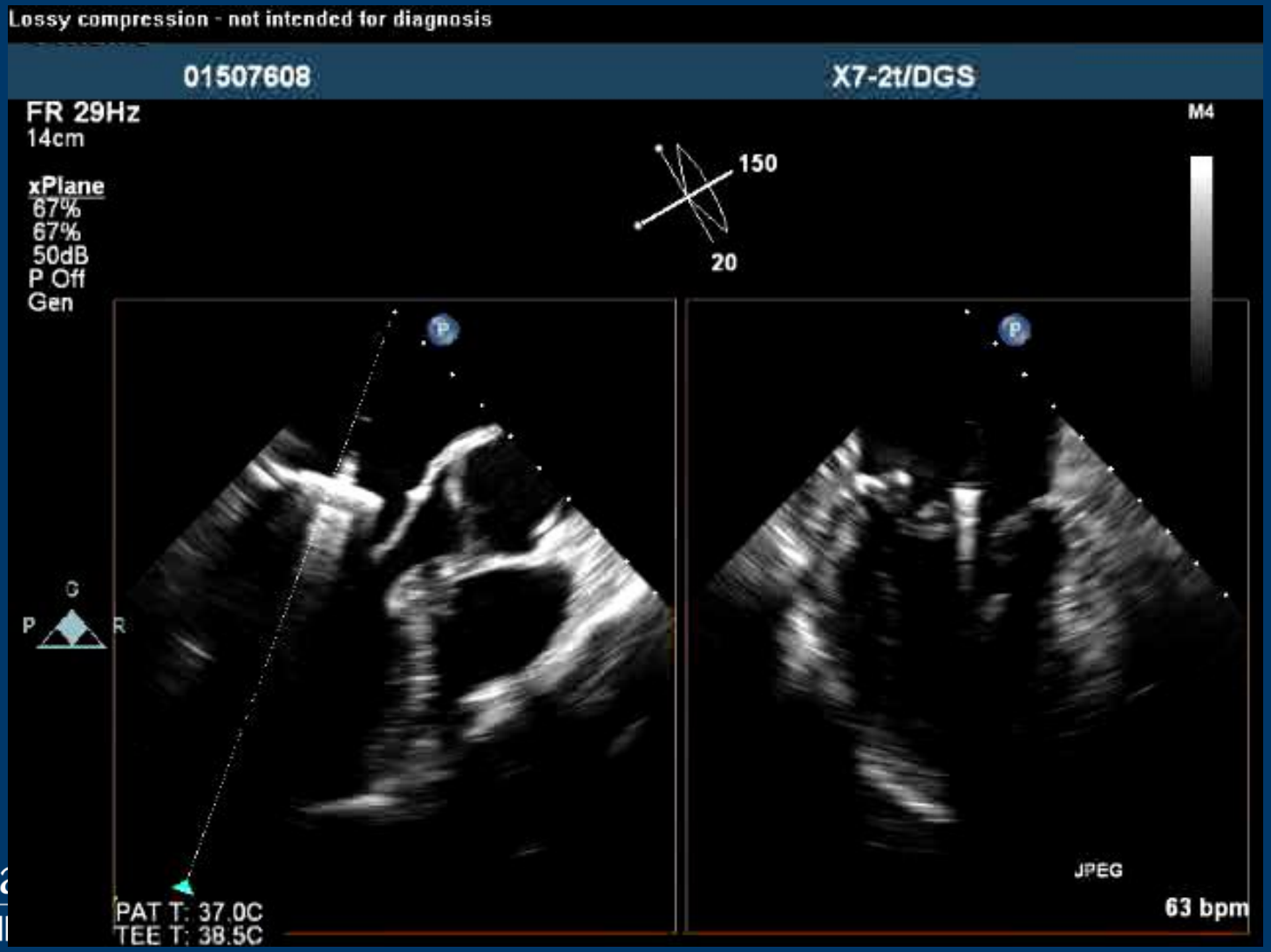


Saint Luke's
MID AMERICA HEART INSTITUTE

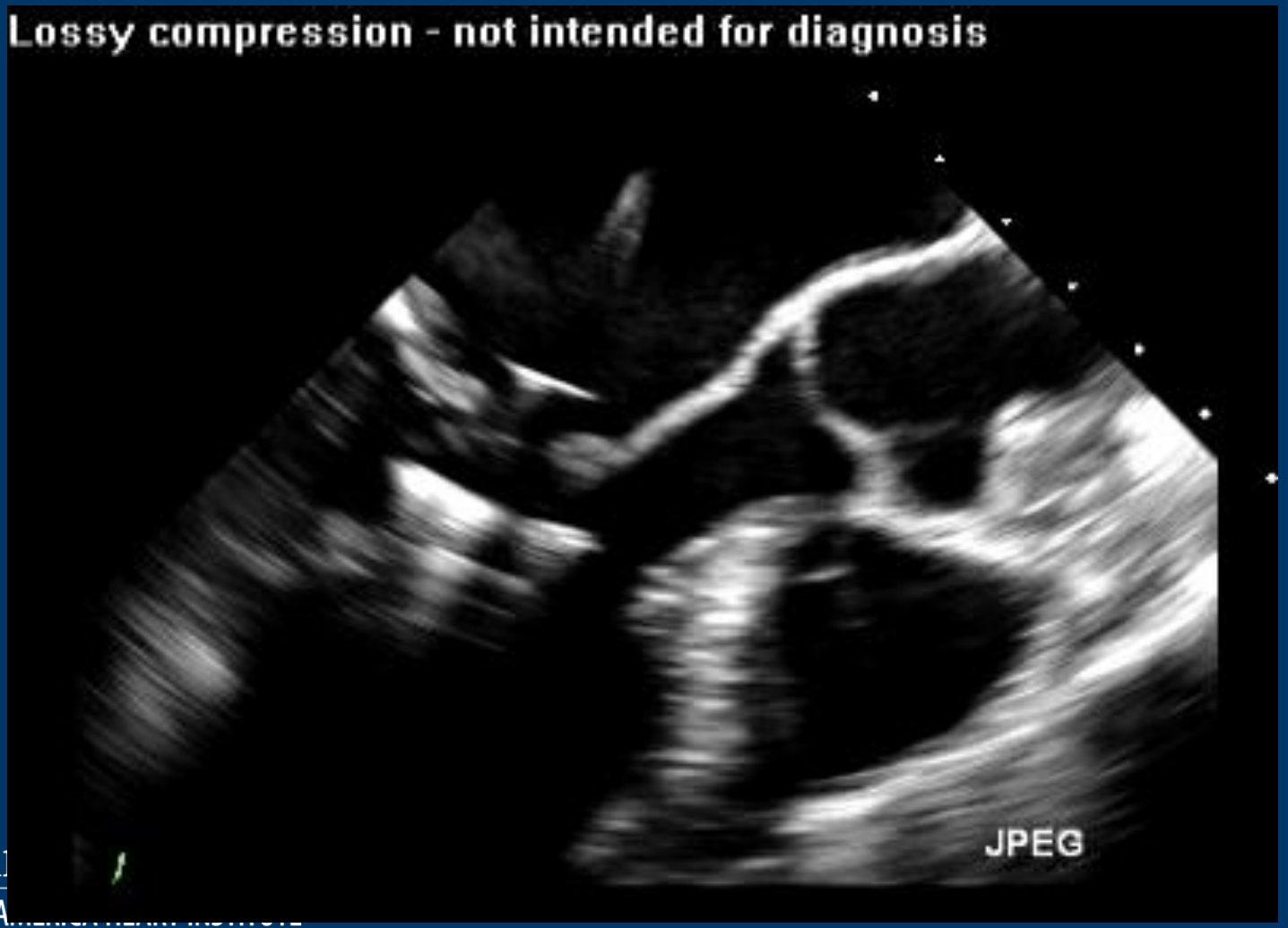
Pre-procedure TEE

Saint Luke's
MID AMERICA HEART INSTITUTE

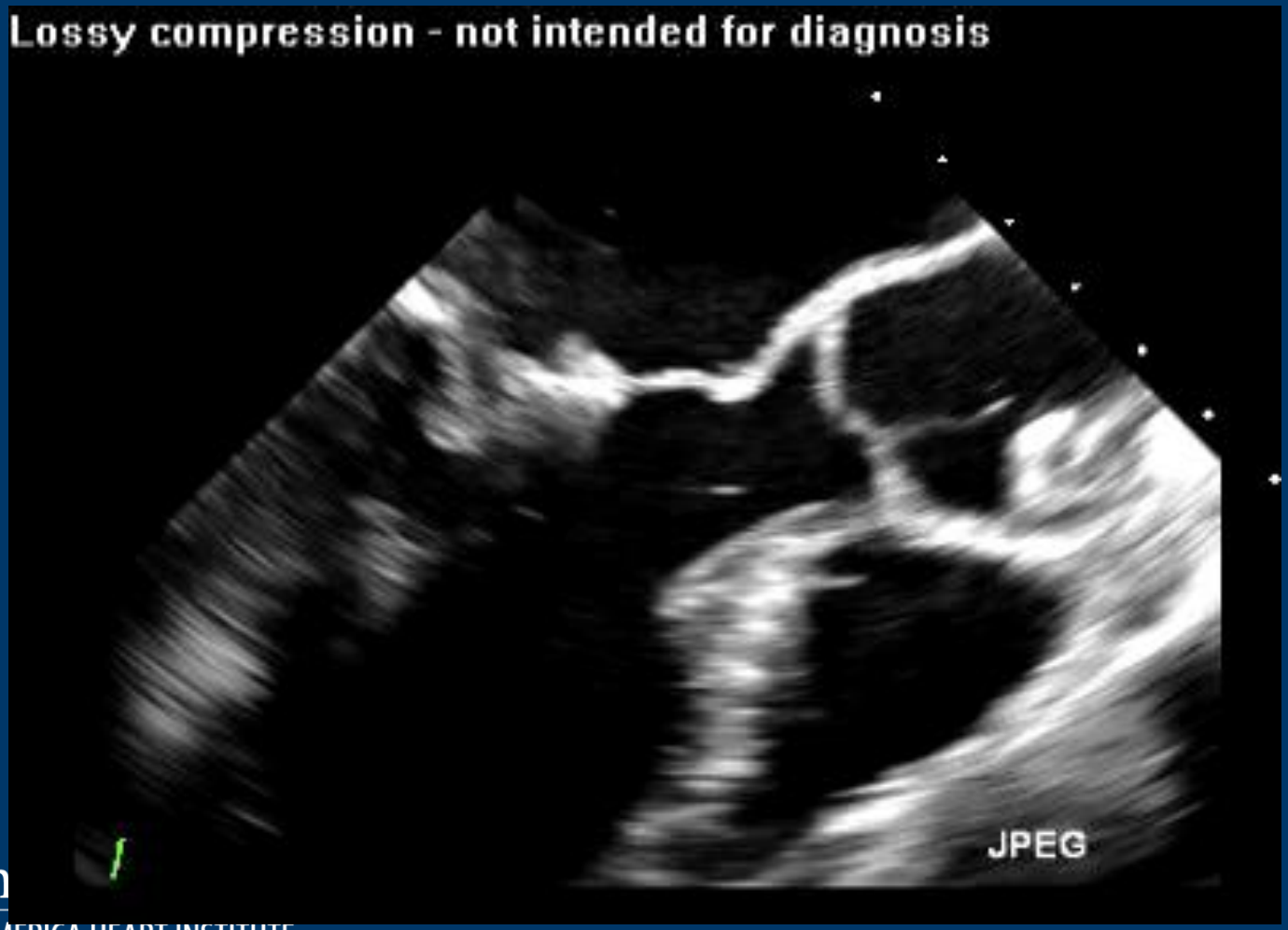
Clip Alignment



Clip in LV

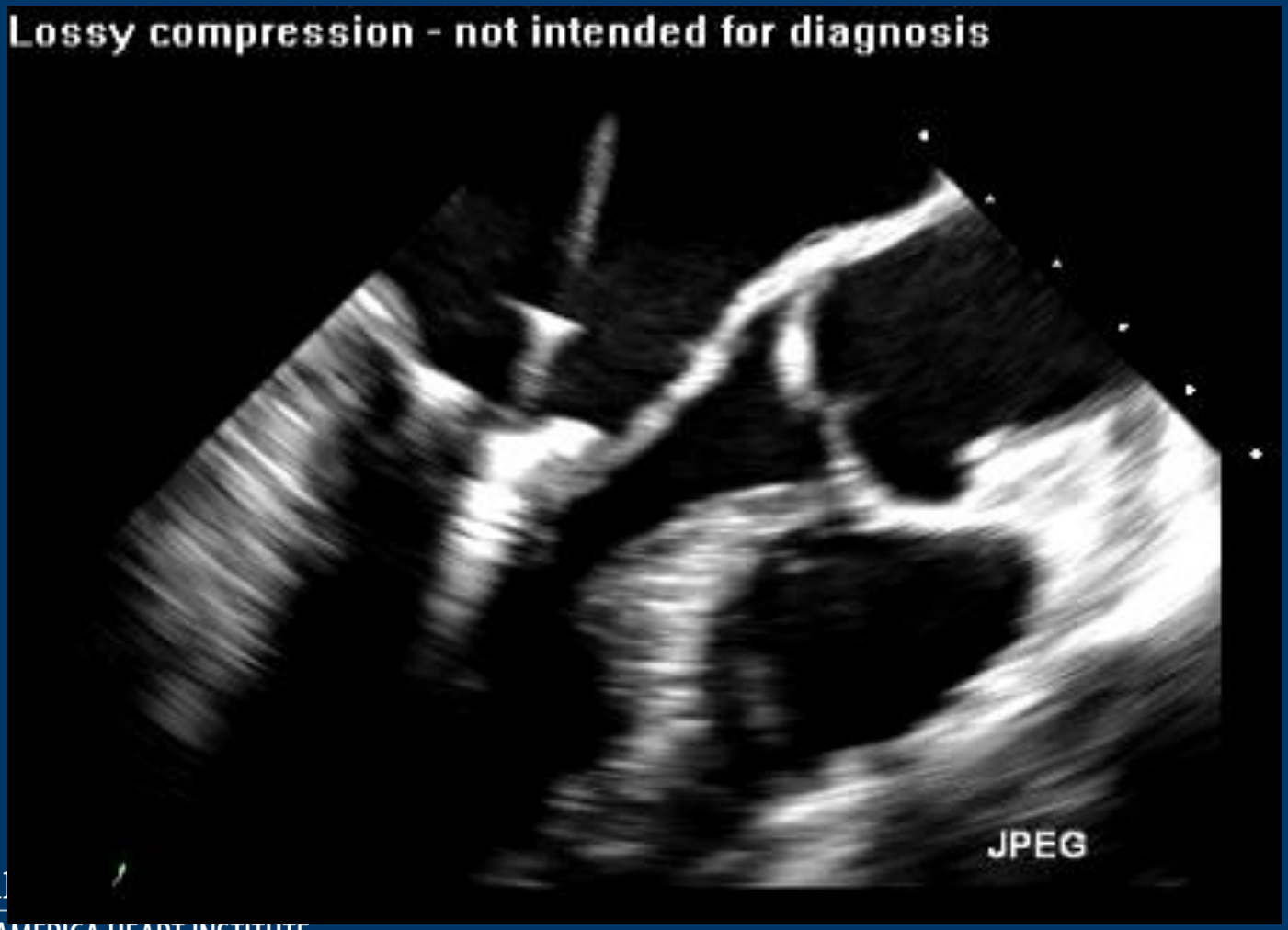


Failed Grasp



Saint
MID AMERICA HEART INSTITUTE

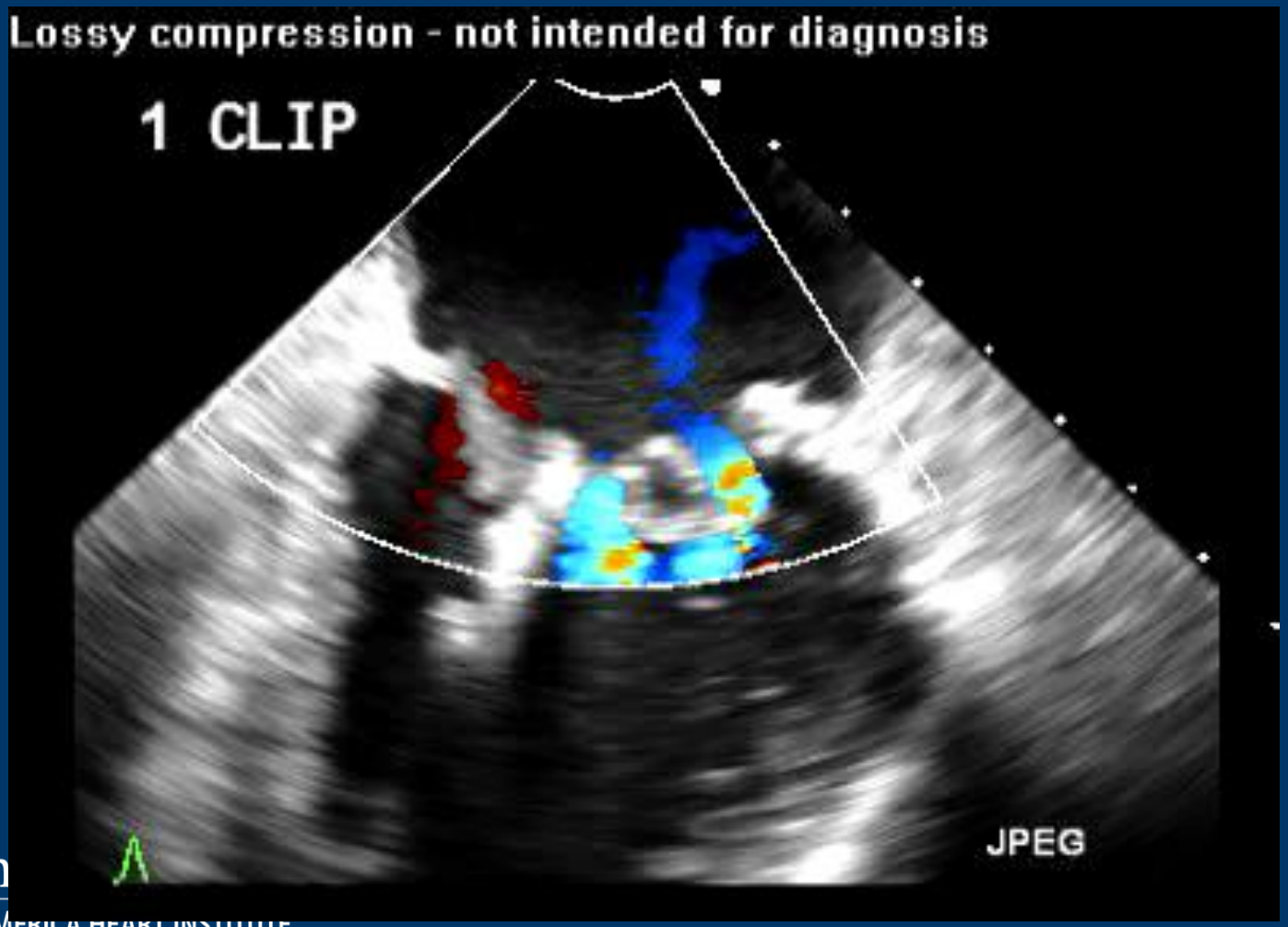
Successful Grasp



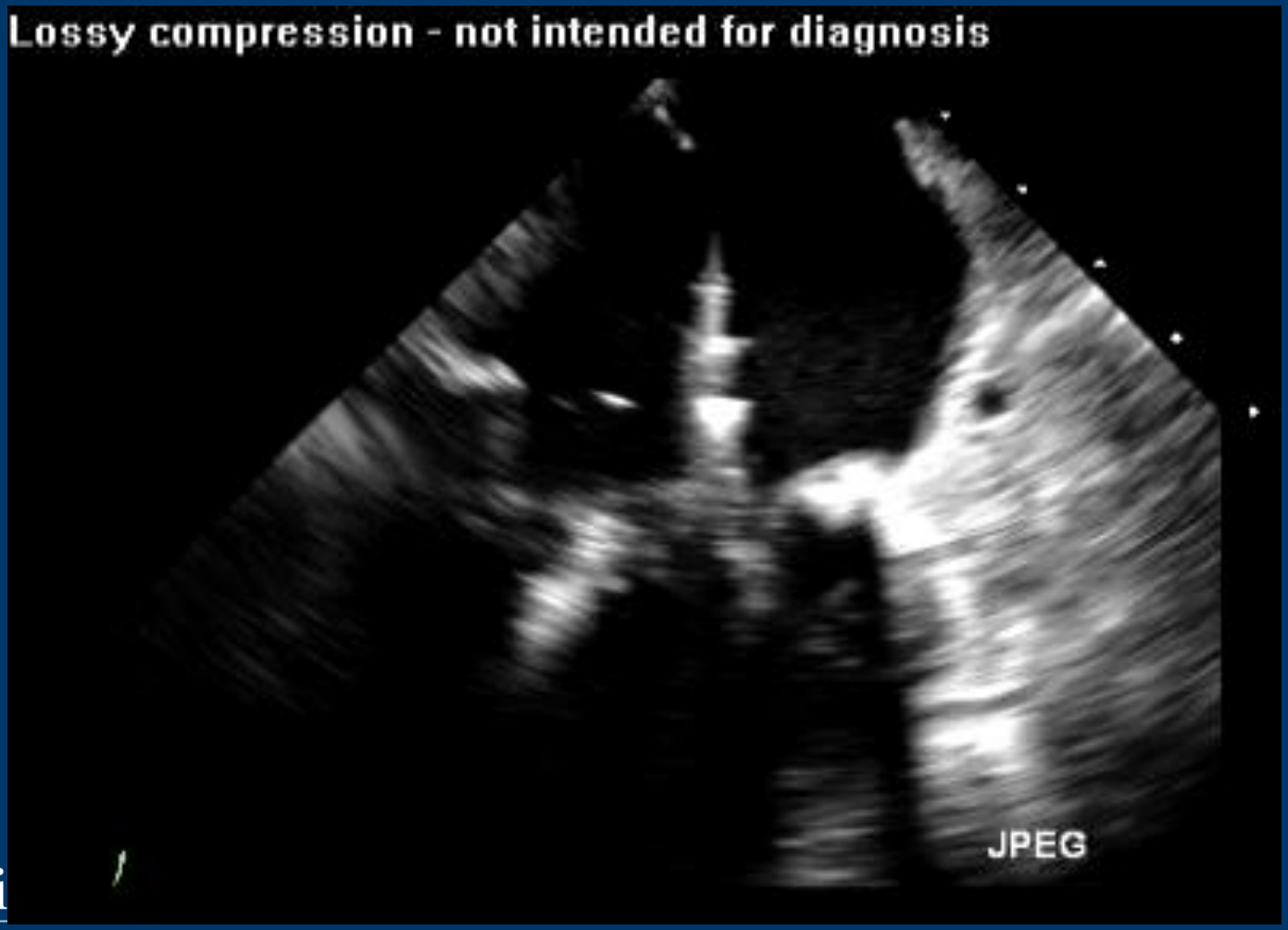
3D Imaging


Lossy compression - not intended for diagnosis
01507608
X7-2t/DGS
FR 42Hz
7.7cm
3D Beats 6
M4
3D
3D 40%
3D 40dB
0
150
180
1 CLIP
JPEG
70 bpm
PAT T: 37.0C
TEE T: 38.7C

Residual MR

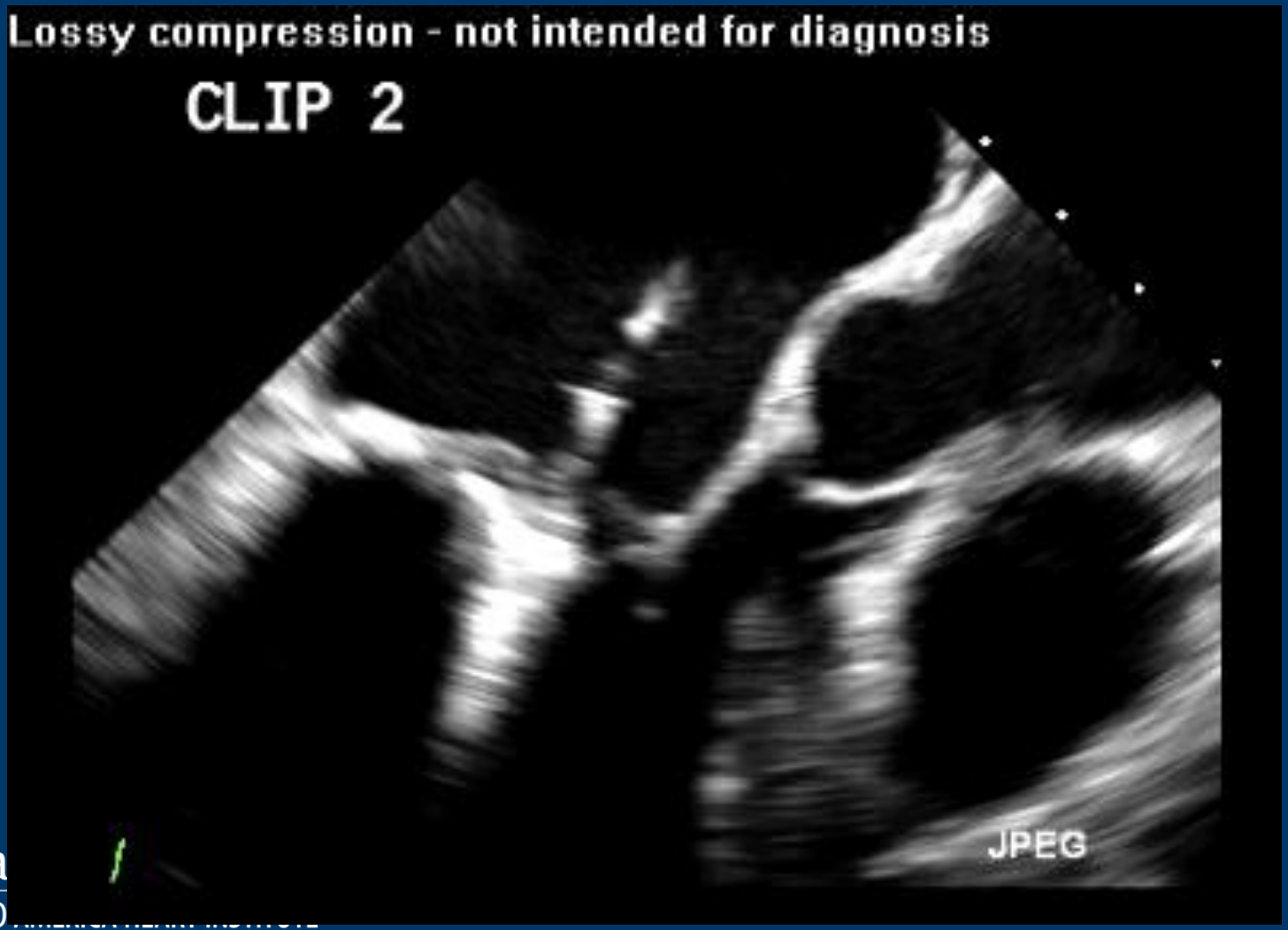


Advancing 2nd Clip

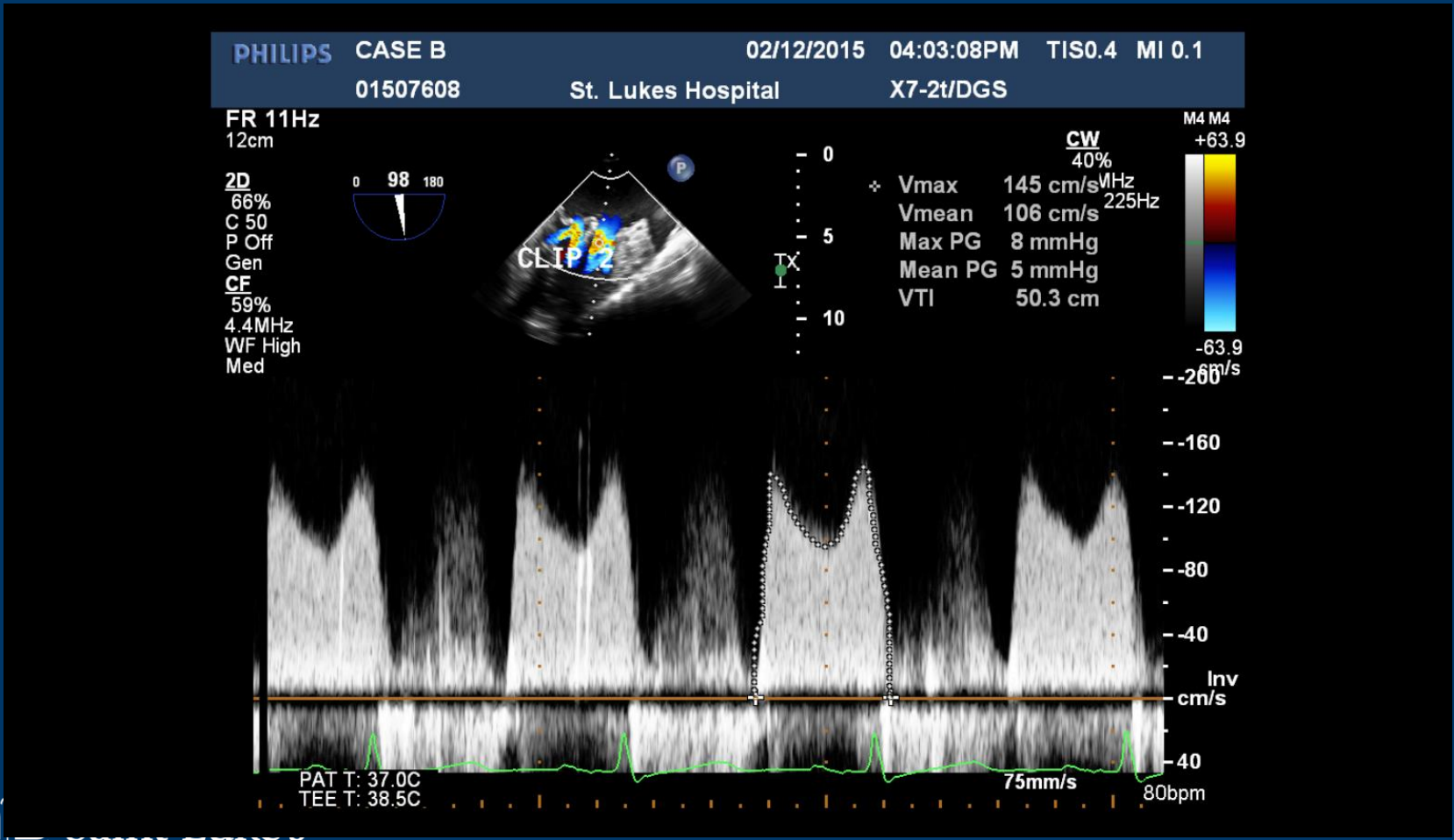


Sai
MID AMERICA HEART INSTITUTE

2nd Grasp

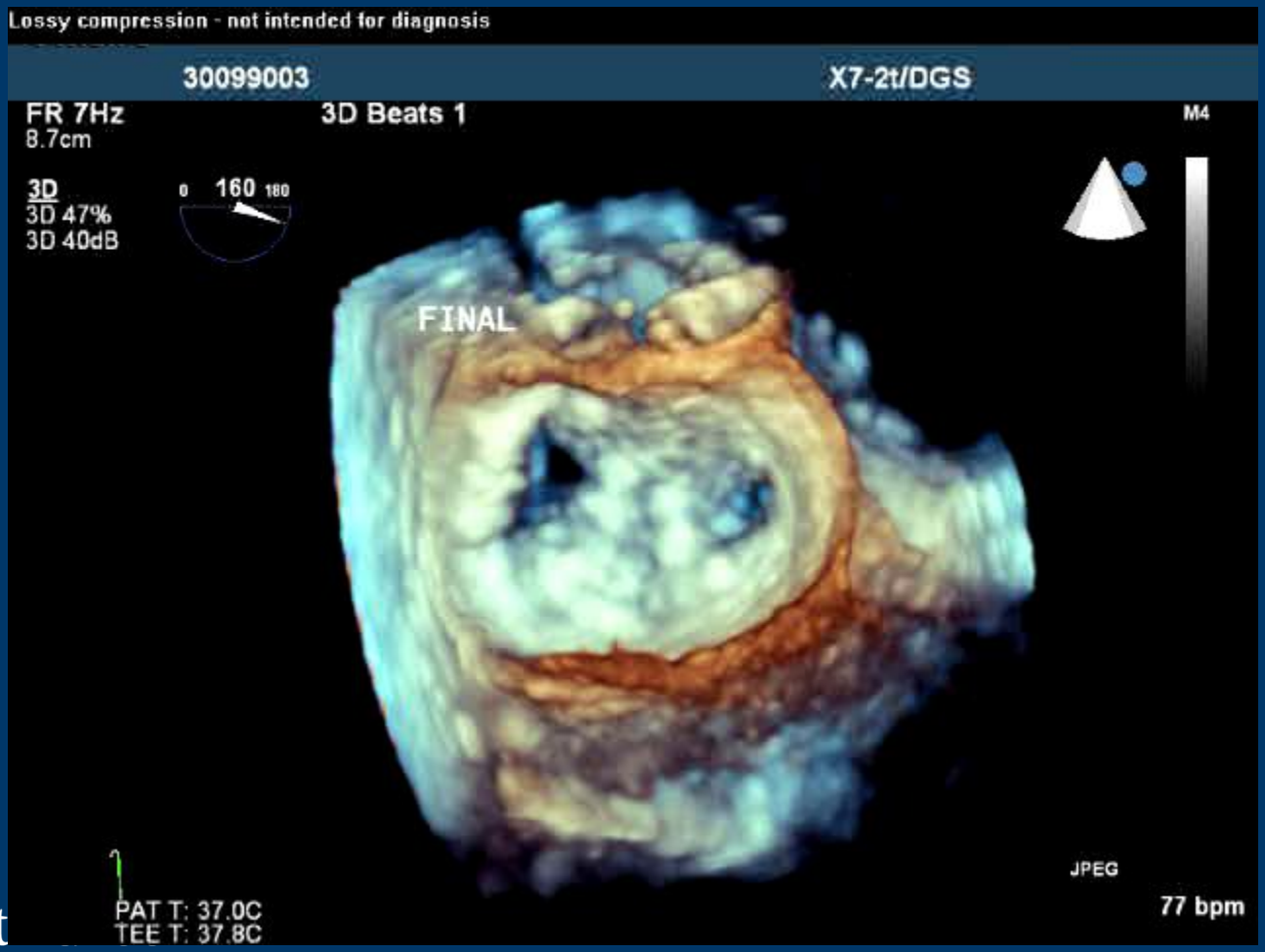


Mitral Valve Gradient



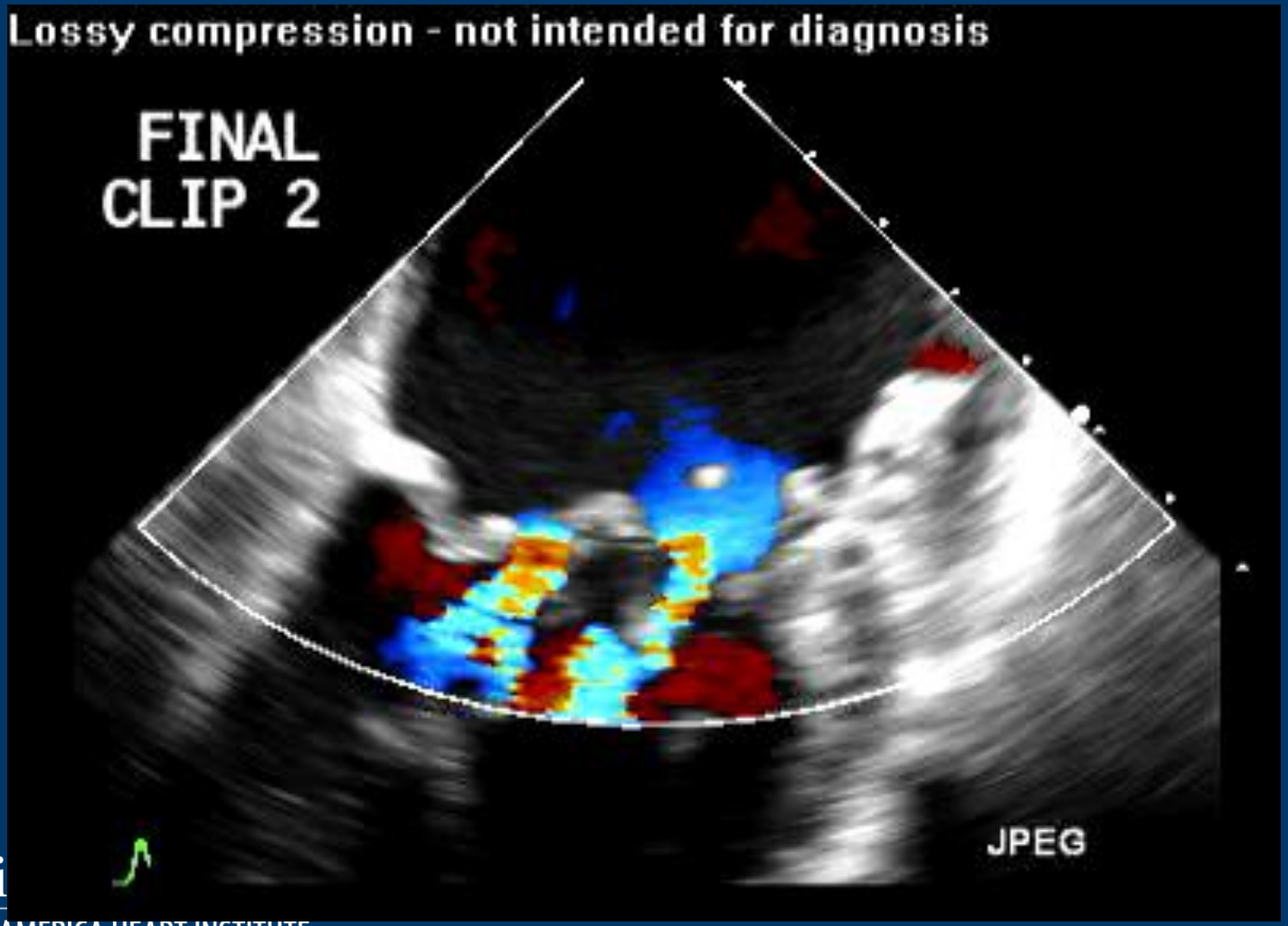
MID AMERICA HEART INSTITUTE

3D imaging – 2 clips



Saint
MID AMERICA HEART INSTITUTE

Final Result



Home the Next Day!

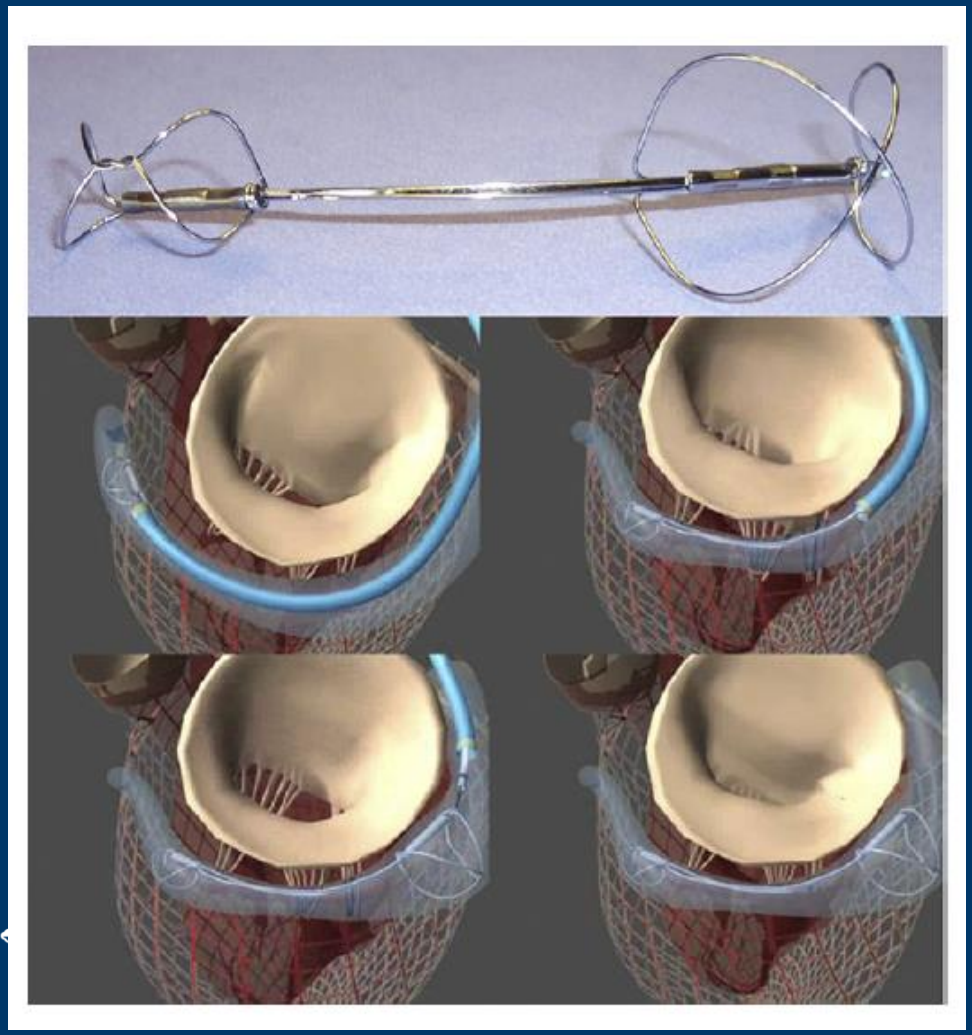
MID AMERICA HEART INSTITUTE

Annuloplasty: Surgical Theory

- **Principles**
  - All valves with significant chronic MR have some degree of annular dilation
  - Re-establishing physiologic configuration of mitral annulus will improve leaflet coaptation
- **Percutaneous Approaches**
  - *Indirect* **:** Implant device within coronary sinus with aim of "pushing" posterior annulus anteriorly
  - *Direct* **:** Device reshapes and cinches mitral annulus directly without involving coronary sinus

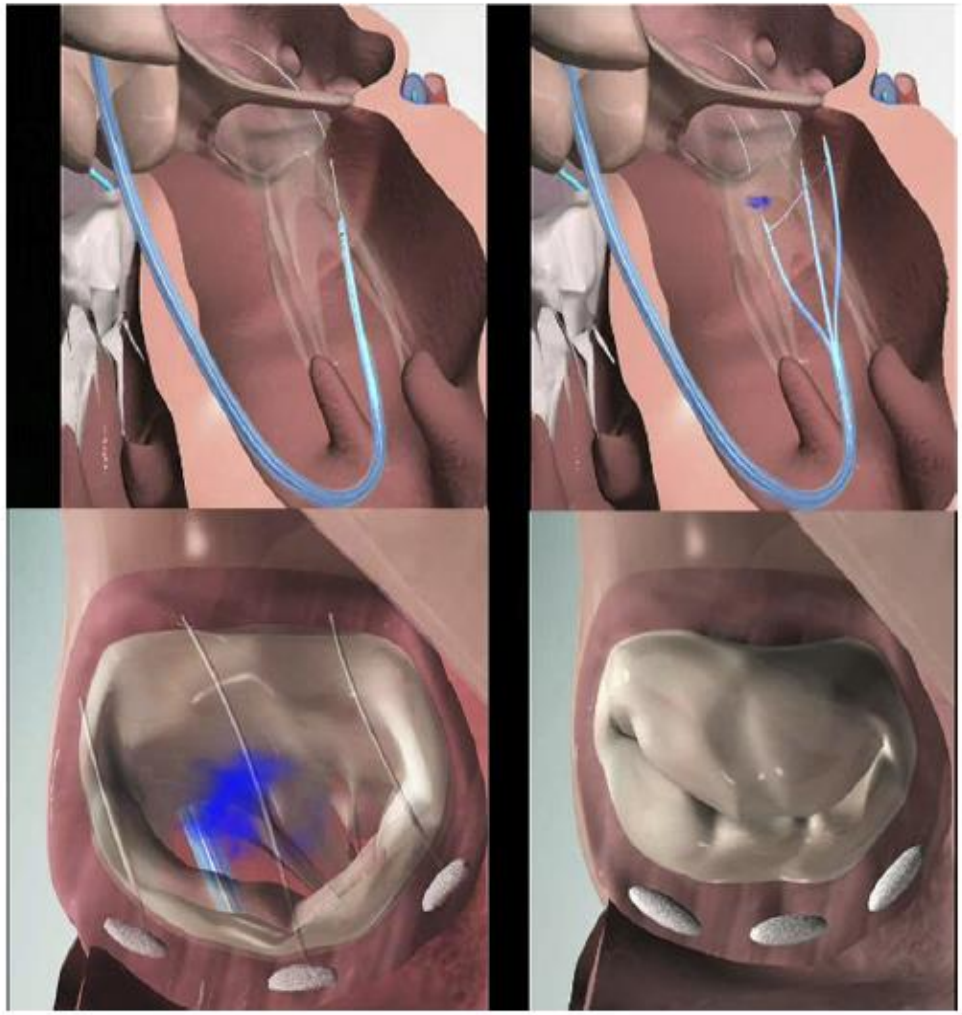
Saint Luke's
MID AMERICA HEART INSTITUTE

Indirect Mitral Annuloplasty
The Carillon XE Device



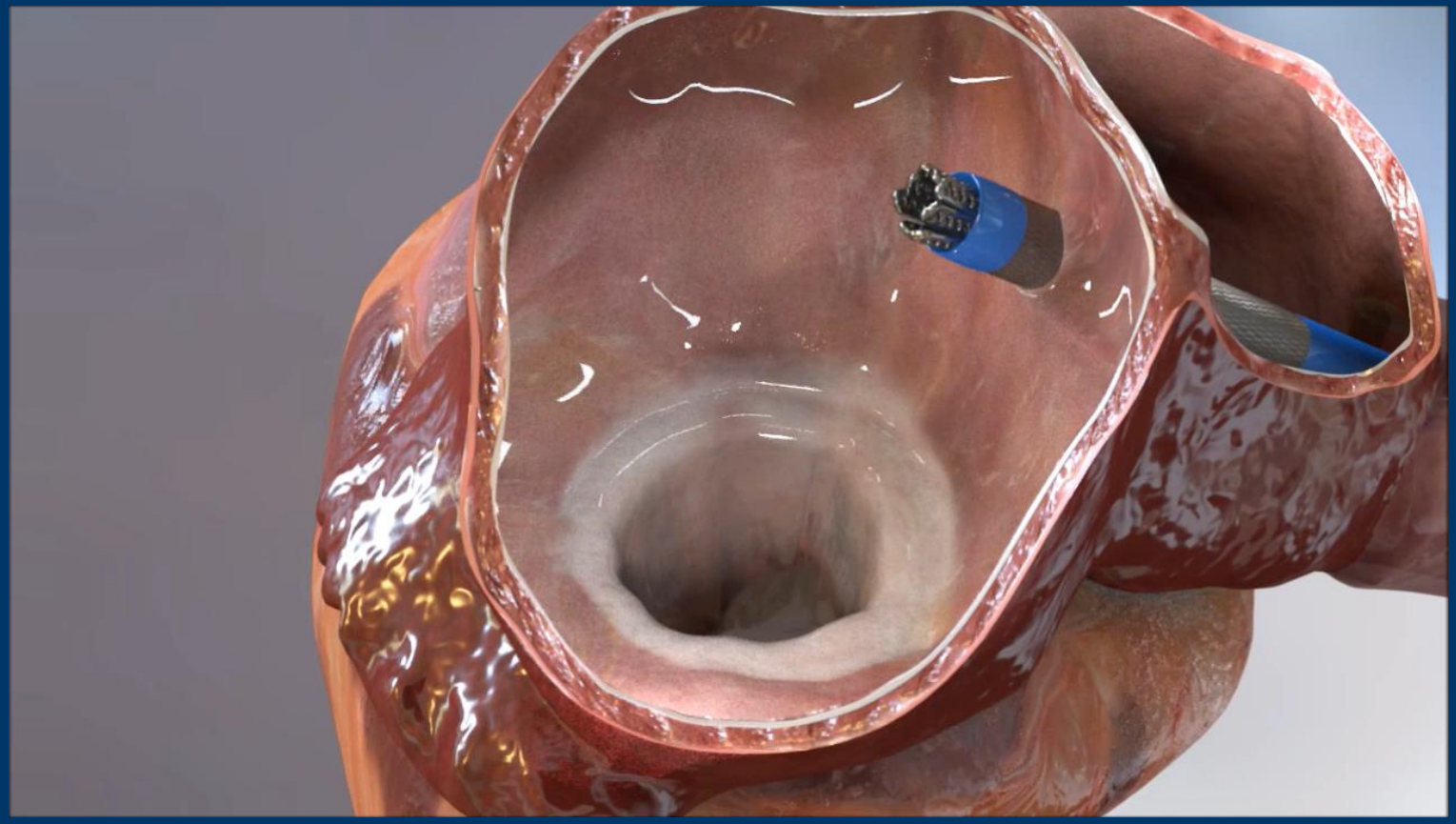
Direct Mitral Annuloplasty: Mechanical Cinching Approach

- **Principle**
  - Devices implanted onto/near annulus and used to directly cinch the annulus
- **Devices**
  - Mitralign
  - Accucinch
  - Cardioband
  - Millipede



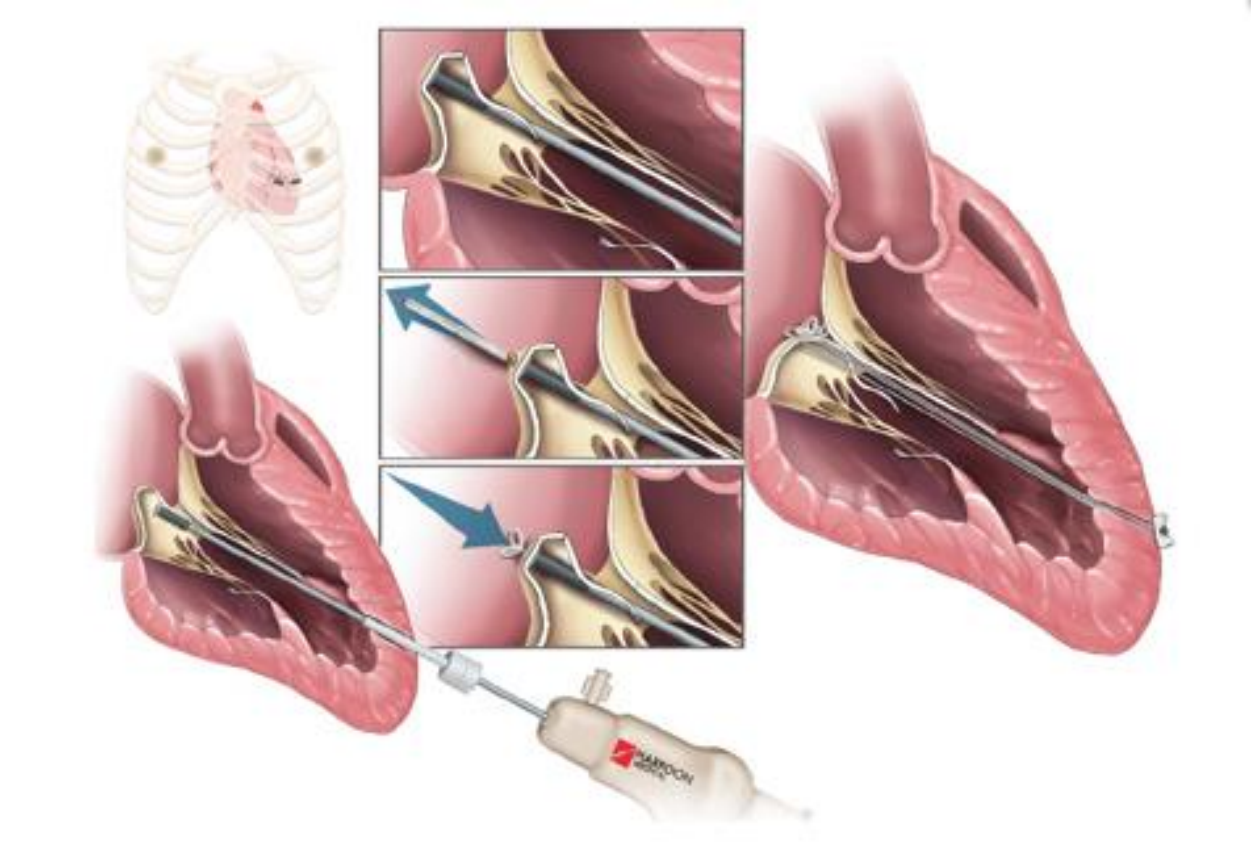
Saint Luke's
MID AMERICA HEART INSTITUTE

Direct Mitral Annuloplasty: Millipede



Saint Luke's
MID AMERICA HEART INSTITUTE

Chordal Reconstruction: Transcatheter Technology



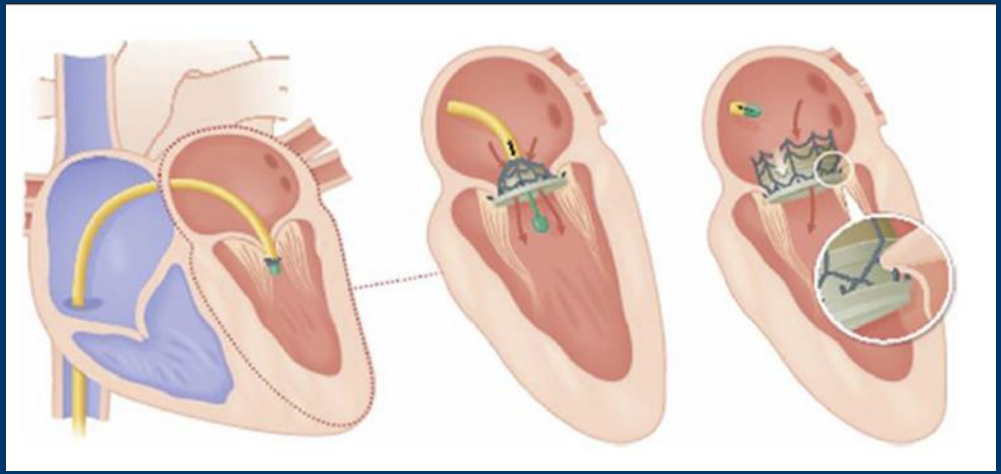
Current Devices

- *NeoChord*
- *MitraFlex*
- *Babic*

Saint Luke's
MID AMERICA HEART INSTITUTE

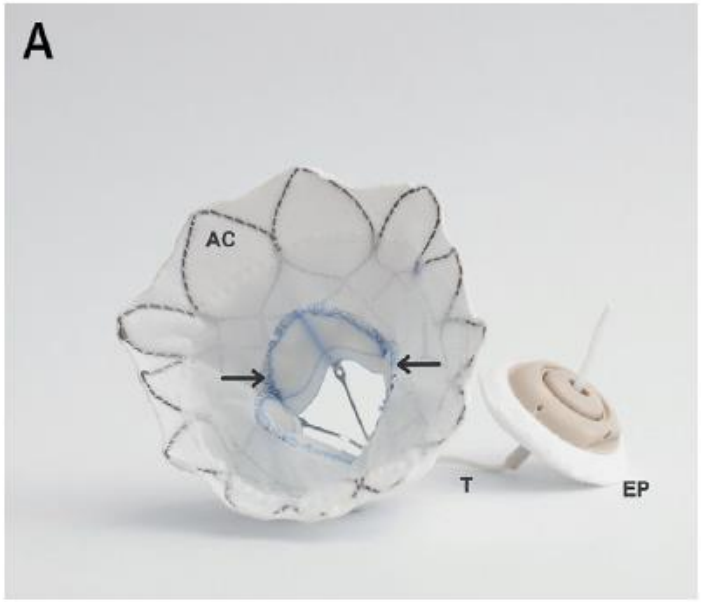
Transcatheter Mitral Valve Replacement

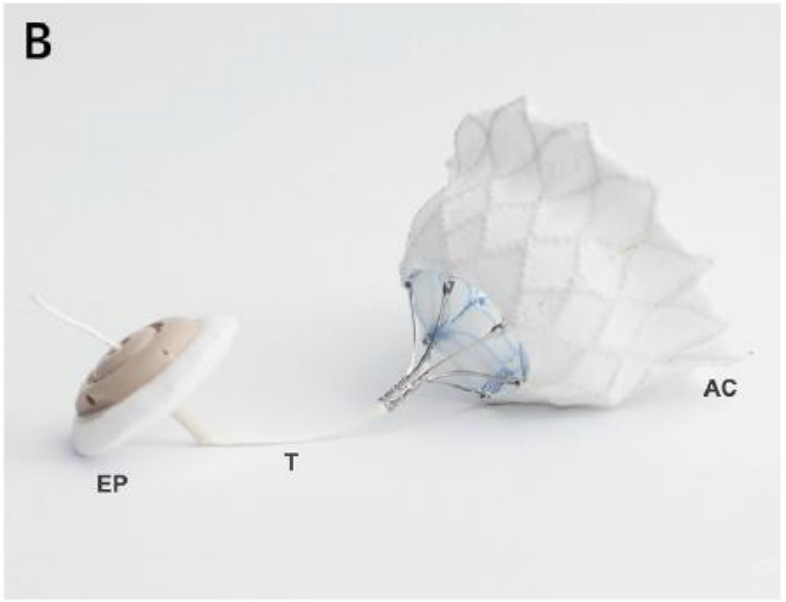
- **Currently in various stages of testing**
  - Tendyne
  - Intrepid
  - M3
- **Involves variety of approaches**
  - Trans-septal
  - Trans-apical
  - Mini-thoractomy
- **Challenges**
  - Risk of paravalvular leaks
  - Possible LVOT obstruction

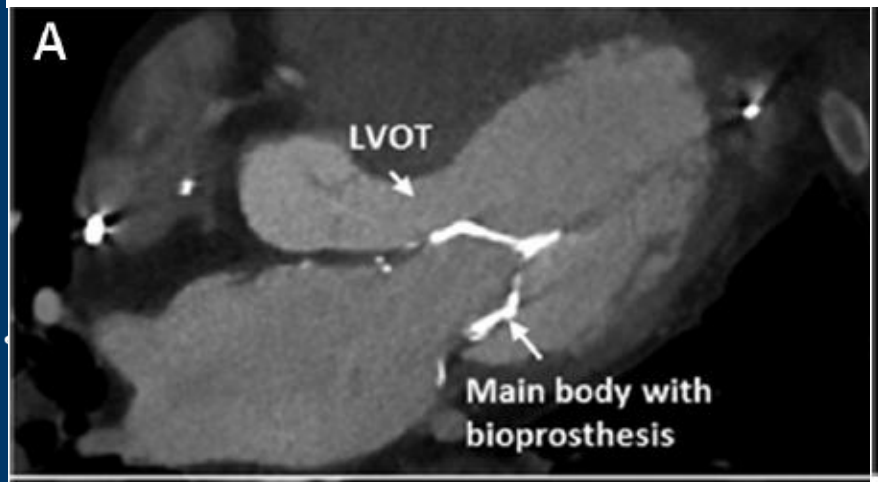


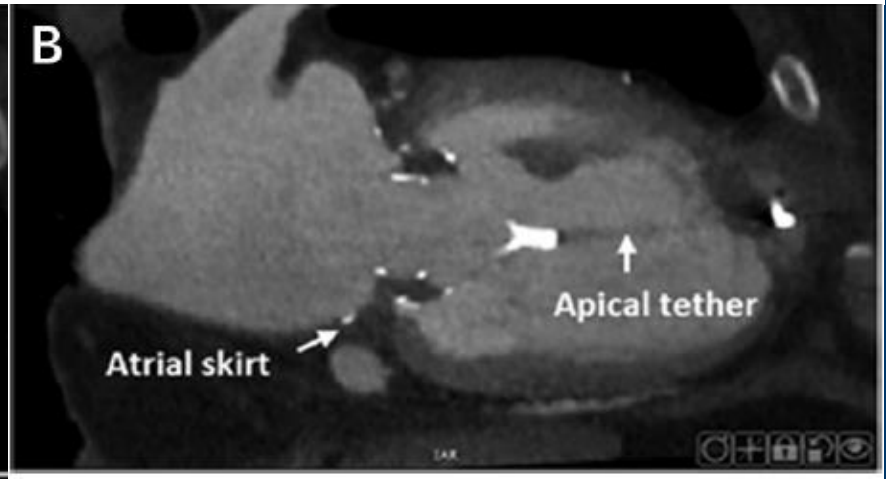
Saint Luke's
MID AMERICA HEART INSTITUTE

TMVR: Tendyne





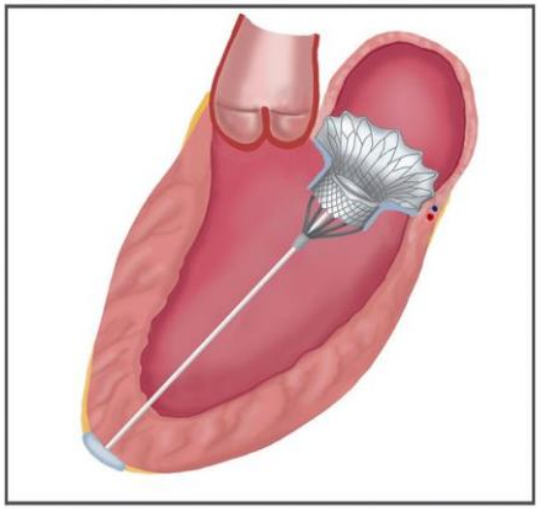




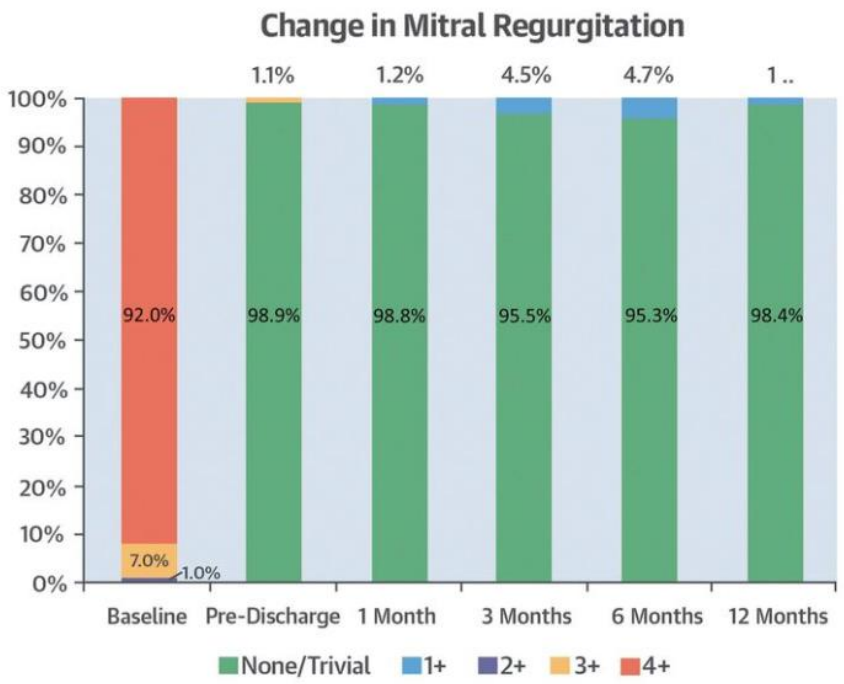
Tendyne: Early Feasibility

CENTRAL ILLUSTRATION: Clinical Outcomes With Transcatheter Mitral Valve Replacement With the Prosthesis

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.

Finding the Right Patient

Conclusions

- TMVr with Mitraclip is approved for treatment of patients with degenerative MR whose surgical risk is high
- Mitraclip is approved for patients with symptomatic functional MR on optimal medical therapy
- Challenges of mitral valve anatomy may make developing a one-size-fits-all strategy difficult
- Many new devices are on the horizon

Saint Luke's
MID AMERICA HEART INSTITUTE

Thank You

Saint Luke's
MID AMERICA HEART INSTITUTE