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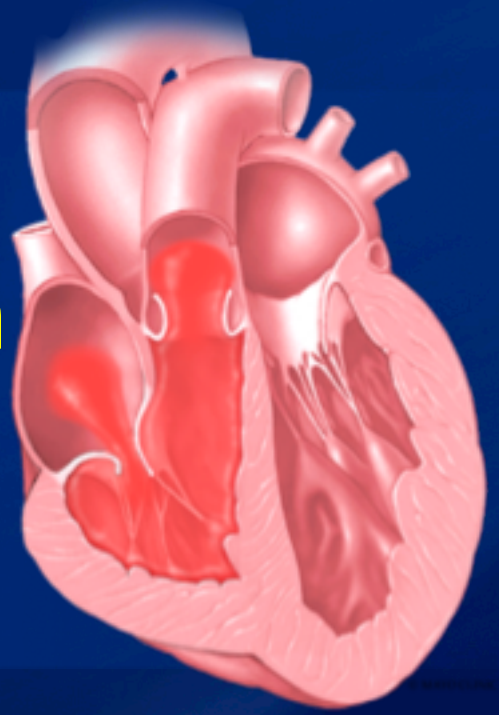
New Interventional Approaches for Treatment of Tricuspid Regurgitation



Mackram F. Eleid, MD

Giornate Cardiologiche Torinesi
October 27, 2018

Disclosures

- Relevant Financial Relationships:
  - None
- Off-Label Use:
  - MitraClip for tricuspid regurgitation (Abbott Vascular)
  - Investigational FORMA repair system (Edwards Lifesciences)
  - TriAlign (Mitralign, MA)

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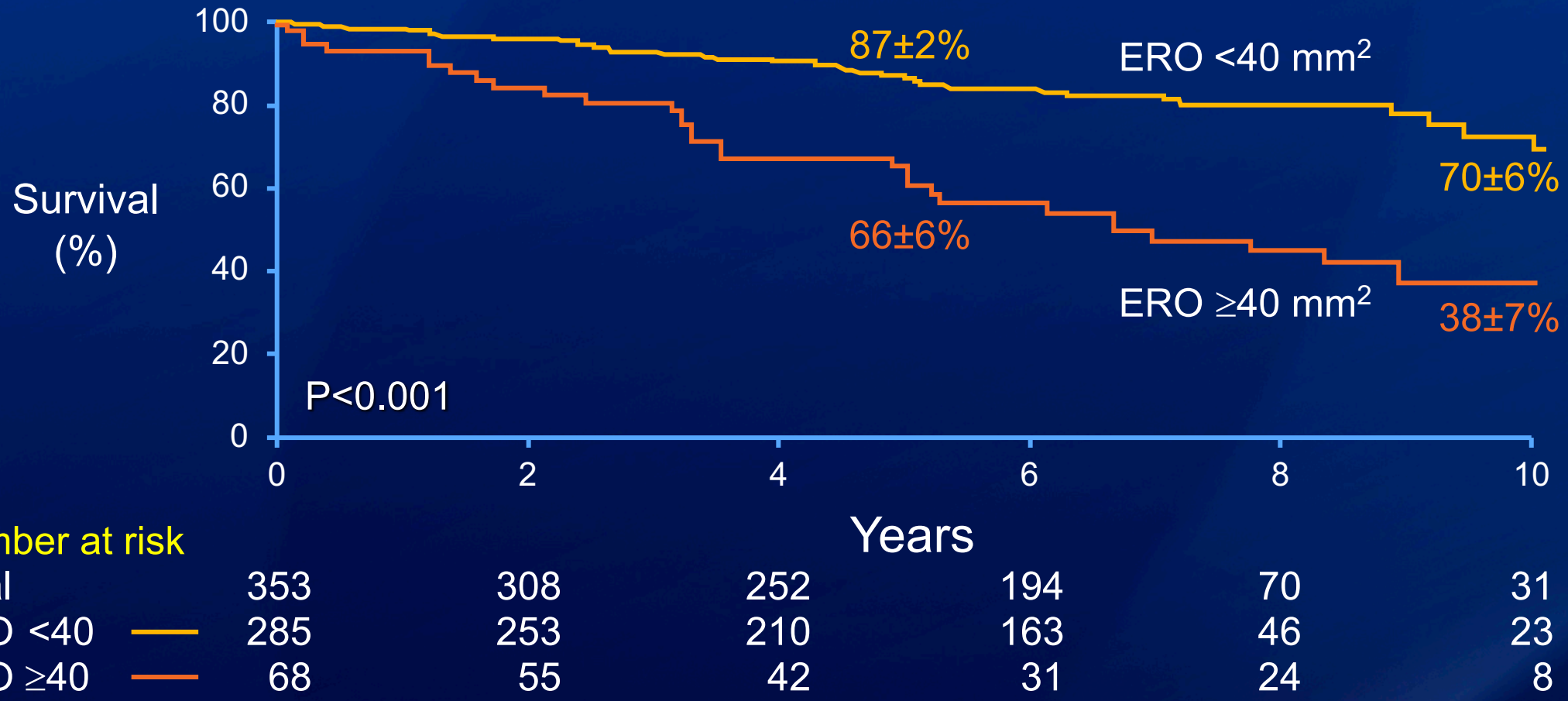
Tricuspid Regurgitation and Survival



Topilsky Y et al: JACC Cardiovasc Img 7(12):1185-94, 2014

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National Trends and Outcomes of Isolated Tricuspid Valve Surgery

- Isolated TV surgery is rarely performed
- In-hospital mortality 8.8%
- In-hospital mortality higher for replacement (11%) vs. repair

Zack CJ…Nishimura RA JACC 2017; 20:2953–2960

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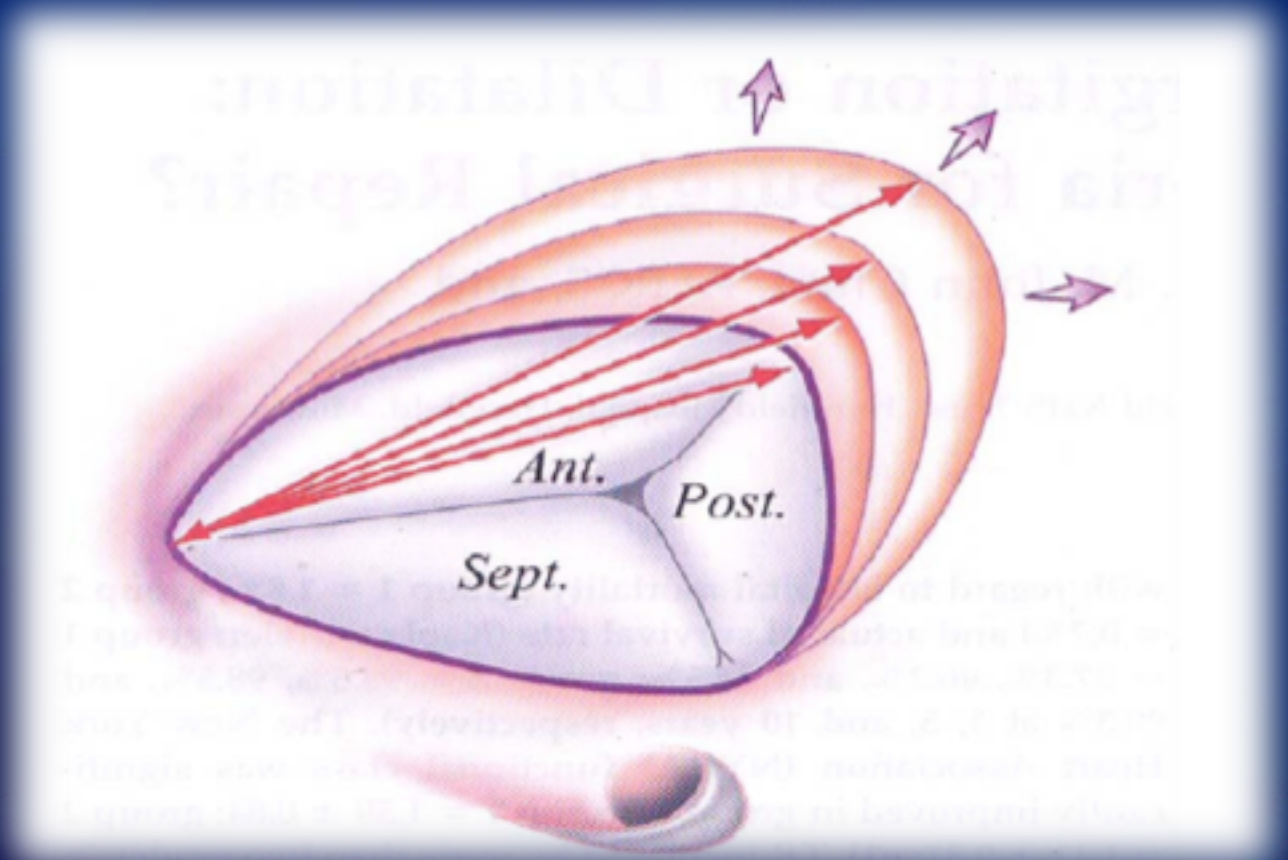
Functional Tricuspid Regurgitation: A Result of Annular Dilatation



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Transcatheter Native TR Therapies

Annuloplasty techniques

- Millipede (Millipede LLC, Ann Arbor, MI)
- Tricinch (4Tech Cardio, Galway, Ireland)
- Cardioband (Edwards Lifesciences, Irvine, CA)
- Trialign (Mitralign Inc, Tewksbury, MA)

Leaflet plication

- MitraClip/TriClip (Abbott, Santa Clara, CA)
- Pascal (Edwars Lifesciences, Irvine, CA)

Spacer

- FORMA (Edwards Lifesciences, Irvine, CA)

Replacement

- Navigate (Navigate Cardiac Structures, Irvin, CA)

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Percutaneous Annuloplasty

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Early Feasibility Study of a Transcatheter Tricuspid Valve Annuloplasty

SCOUT Trial 30-Day Results

Rebecca T. Hahn, MD,[a,b] Christopher U. Meduri, MD,[c] Charles J. Davidson, MD,[d] Scott Lim, MD,[e] Tamim M. Nazif, MD,[a] Mark J. Ricciardi, MD,[d] Vivek Rajagopal, MD,[d] Gorav Ailawadi, MD,[e] Mani A. Vannan, MBBS,[c] James D. Thomas, MD,[d] Dale Fowler, MD,[e] Stuart Rich, MD,[d] Randy Martin, MD,[c] Geraldine Ong, MD,[b] Adam Groothuis, PhD,[f] Susheel Kodali, MD[a]

BACKGROUND The SCOUT (Percutaneous Tricuspid Valve Annuloplasty System for Symptomatic Chronic Functional Tricuspid Regurgitation) trial is a prospective, single-arm, multicenter, early feasibility study of a novel transcatheter device to plicate the tricuspid annulus (TA) and reduce tricuspid regurgitation (TR).

OBJECTIVES This study tested the feasibility and safety of a novel transcatheter device and assessed its early performance and functional outcomes.

METHODS Between November 2015 and June 2016, 15 patients with New York Heart Association (NYHA) functional class ≥II and moderate or greater functional TR were enrolled. Primary performance and safety endpoint outcomes were technically successful at 30 days with no reintervention. Echocardiographic measurements (TA diameter, effective regurgitant orifice area [EROA], left ventricular stroke volume [LVSV]) and quality-of-life (QoL) measurements (NYHA functional class, Minnesota Living with Heart Failure Questionnaire [MLHFQ], and 6-min walk test [6MWT]) were performed at baseline and 30 days.

RESULTS All patients (mean 73.2 ± 6.9 years of age, 87% female) underwent successful device implantation with no deaths, strokes, bleeding, tamponade, or valve reintervention. Technical success rate at 30 days was 80%, with 3 single-pledget annular detachments without reintervention. In the remaining 12 patients, there were significant reductions in TA (12.3 ± 3.1 cm^2 to 11.3 ± 2.7 cm^2, respectively; $p = 0.019$) and EROA (0.51 ± 0.18 cm^2 vs. 0.32 ± 0.18 cm^2, respectively; $p = 0.020$), with significant increase in LVSV (63.6 ± 17.9 ml vs. 71.5 ± 25.7 ml, respectively; $p = 0.021$). In the intention-to-treat cohort, there were significant improvements in NYHA functional class (≥1 class, $p = 0.001$), MLHFQ (47.4 ± 17.6 to 20.9 ± 14.8; $p < 0.001$), and 6MWT (245.2 ± 110.1 to 298.0 m ± 107.6 m; $p = 0.008$).

CONCLUSIONS The 30-day results of the SCOUT trial confirmed the safety of the novel transcatheter device, which reduced TA and EROA, increased LVSV, and improved QoL. (Early Feasibility of the Mitralign Percutaneous Tricuspid Valve Annuloplasty System (PTVAS) Also Known as TriAlign [SCOUT]; NCT02574650.) (J Am Coll Cardiol 2017;69:1795-806)

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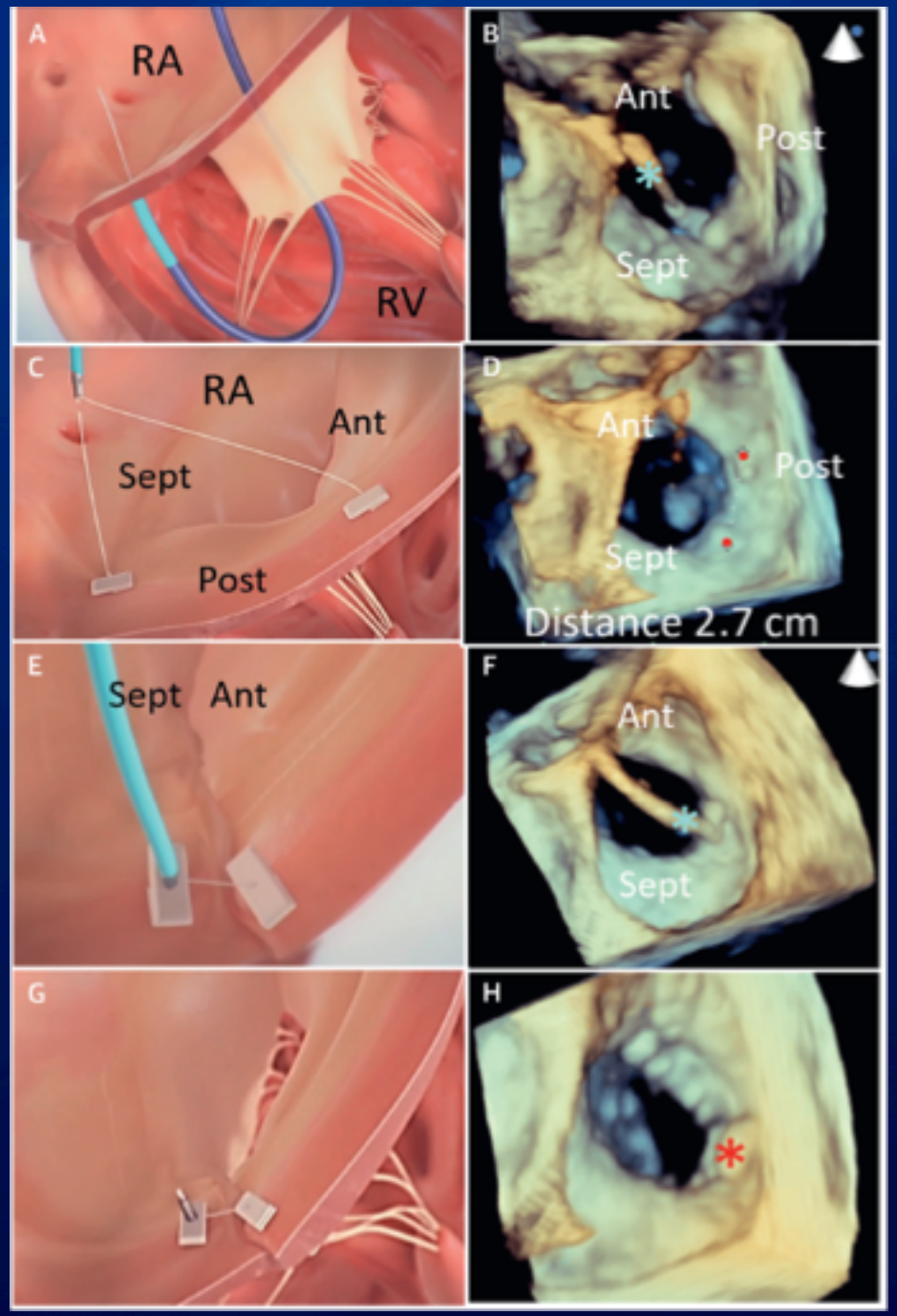

Transjugular Delivery of radiofrequency wire across annulus

Placement of two pledgeted sutures

Plication of two pledgeted sutures

Bicuspidized valve

Hahn RT et al. J Am Coll Cardiol 2017;69:1795-806.

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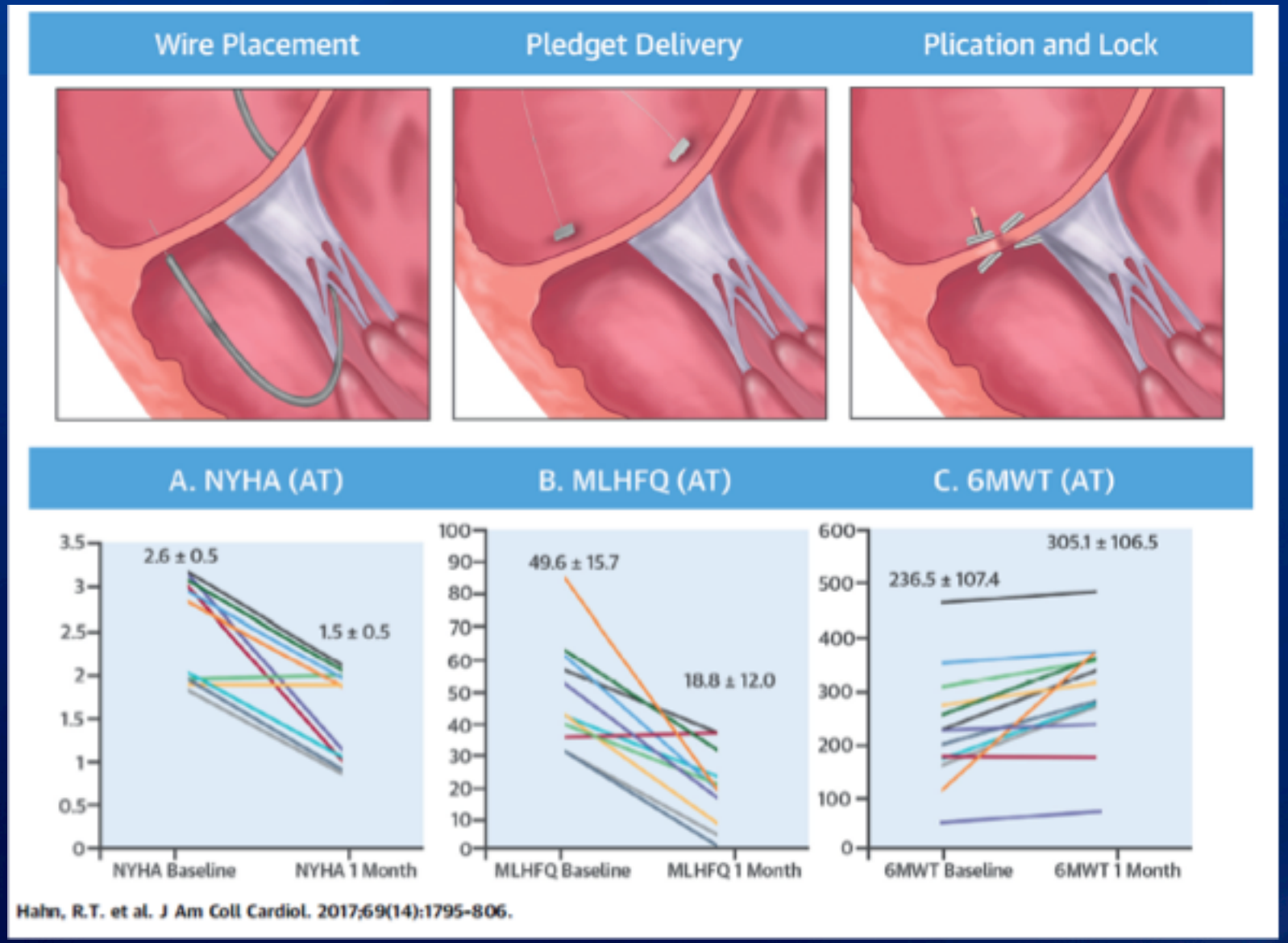
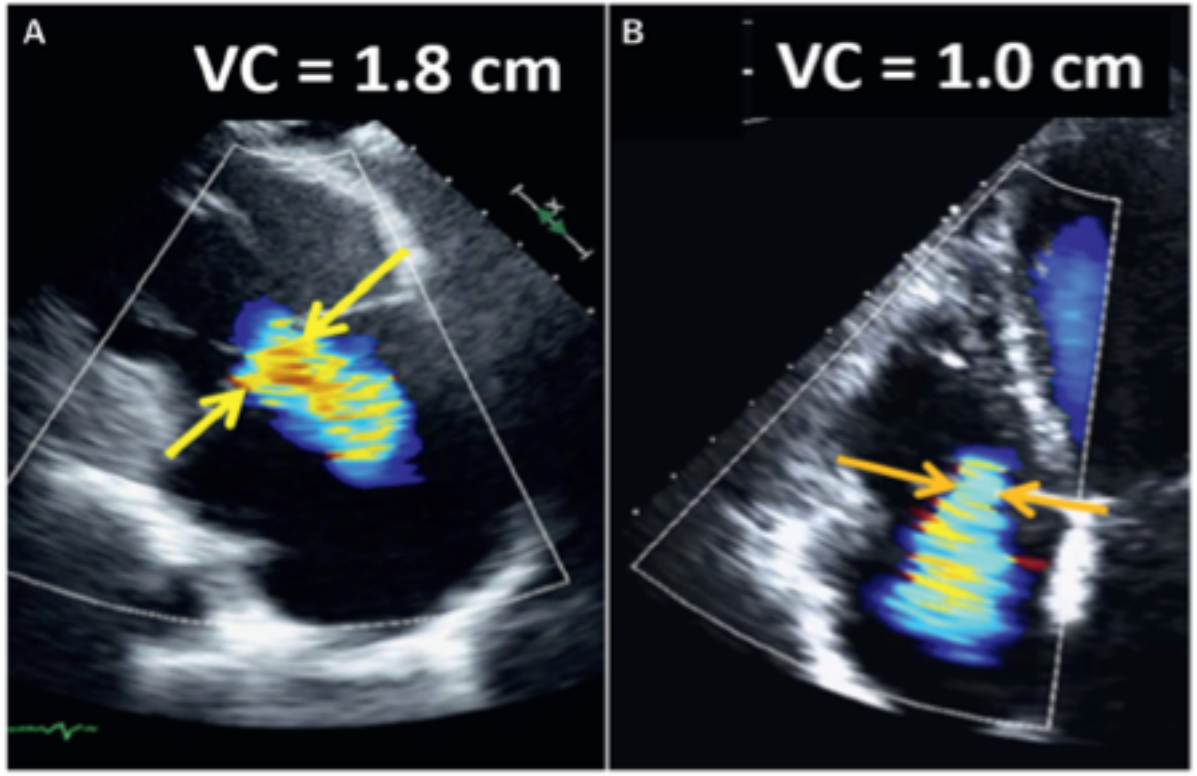


Hahn RT et al. J Am Coll Cardiol 2017;69:1795-806.

FIGURE 1 Vena Contracta Measurements



Representative maximum **(A)** and minimum **(B)** VC measurements are shown. The noncircular nature of the tricuspid orifice is clear from the differences in these measurements. VC = vena contracta.

Hahn RT et al. J Am Coll Cardiol 2017;69:1795-806.

Procedural Data

TABLE 2 Procedural Data of the 15 Patients Enrolled in the SCOUT Trial

Total procedure time, min	124 ± 62
Total contrast volume, ml	51.4 ± 58.0
Total fluoroscopy time, min	96.2 ± 30.8
Total general anesthesia time, min	352.9 ± 69.0
Vascular access site closure	
Manual compression	11 (73.3)
Vascular closure device	2 (13.3)
Permanent implantation of device in the correct position	15 (100.0)
Plication performed	15 (100.0)
Pledget detachment	1 (6.7)
Bleeding/access site complications	0 (0.0)
MACE	1 (6.7)
Tamponade	0 (0.0)

Values are mean ± SD or n (%). MACE = major adverse cardiac events: death, nonfatal myocardial infarction, or revascularization.

TABLE 3 Measures of Technical Success

	30-Day Outcome
Overall technical success	12/15 (80.0)
Successful access, delivery, and retrieval of the system	15/15 (100.0)
Deployment and correct positioning of device	12/15 (80.0)
No unplanned or emergency surgery or reintervention related to the device or access procedure within 30 days	14/15 (93.3)
Freedom from mortality within 30 days	15/15 (100.0)

Values n/N (%).

- 3 patients (20%) experienced single-pledget annular detachments at 30 days

Hahn RT et al. J Am Coll Cardiol 2017;69:1795-806.

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ORIGINAL RESEARCH ARTICLE

Transcatheter Treatment of Severe Tricuspid Regurgitation with the Edge-to-Edge: MitraClip Technique

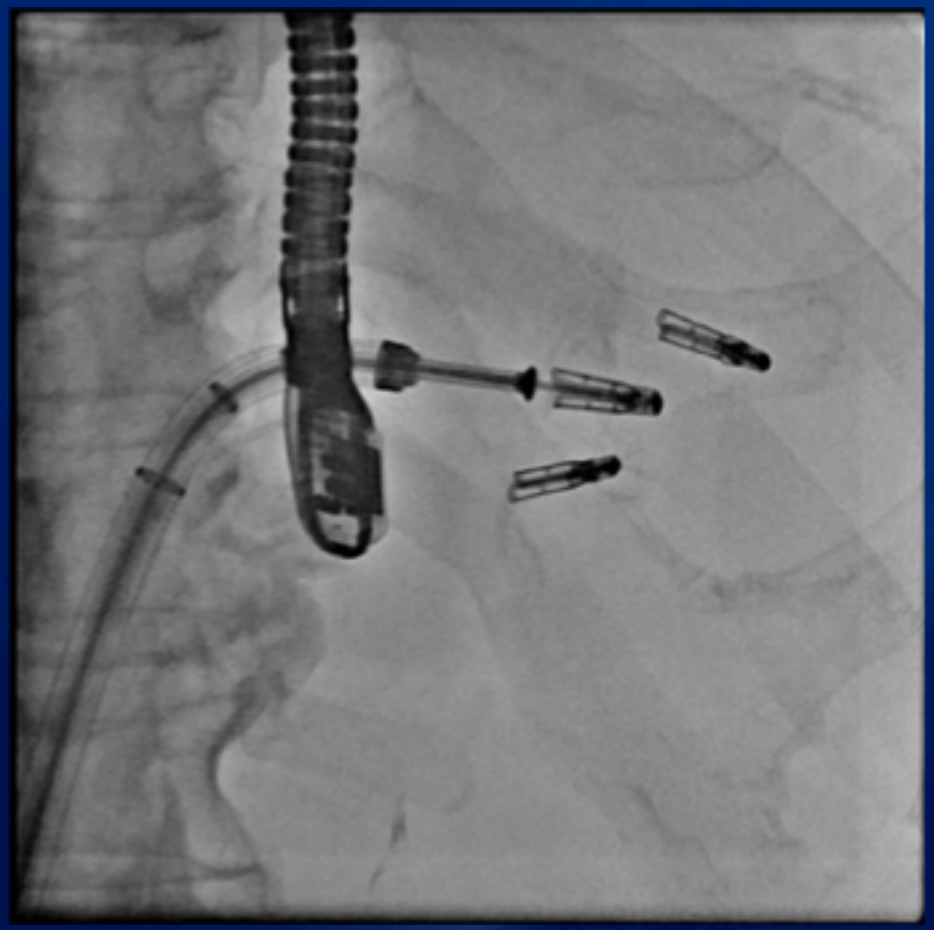
Georg Nickenig, Marek Kowalski, Jörg Hausleiter, Daniel Braun, Joachim Schofer, Ermela Yzeiraj, Volker Rudolph, Kai Friedrichs, Francesco Maisano, Maurizio Taramasso, Neil P. Fam, Giovanni Bianchi, Francesco Bedogni, Paolo Denti, Ottavio Alfieri, Azeem Latib, Antonio Colombo, Christoph Hammerstingl, Robert Schueler

Background—Current surgical and medical treatment options for severe tricuspid regurgitation (TR) are limited and additional interventional approaches are required. In the present observational study, the safety and feasibility of transcatheter repair of chronic severe TR with the MitraClip system were evaluated. In addition, the effects on clinical symptoms were assessed.

Methods—Patients with heart failure symptoms and severe TR on optimal medical treatment were treated with the MitraClip system. Safety, defined as periprocedural adverse events such as death, myocardial infarction, stroke, or cardiac tamponade, and feasibility, defined as successful implantation of one or more MitraClip devices and reduction of TR by at least one grade, were evaluated before discharge and after 30 days. In addition, functional outcome, defined as changes in NYHA class and 6 minutes walking distance, were assessed.

Results—We included 64 consecutive patients (mean age 76.6±10 years) deemed unsuitable for surgery who underwent MitraClip treatment for chronic, severe TR for compassionate use. Functional TR was present in 88%. 22 patients were also treated with the MitraClip system for mitral regurgitation as a combined procedure. The degree of TR was severe or massive in 88% of patients before the procedure. The MitraClip device was successfully implanted in the tricuspid valve in 97% of the cases. After the procedure, TR was reduced by at least one grade in 91% of the patients, thereof 4% that were reduced from massive to severe. In a total of 13% of patients TR remained severe after the procedure. Significant reductions in effective regurgitant orifice area (0.9±0.3cm²vs.0.4±0.2cm²; p<0.001), vena contracta width (1.1±0.5cm vs. 0.6±0.3cm; p=0.001) and regurgitant volume (57.2±12.8ml/beat vs. 30.8±6.9ml/beat; p<0.001) were observed. No intraprocedural deaths, cardiac tamponade, emergency surgery, stroke, myocardial infarction or major vascular complications occurred. There were 3 (5%) in-hospital deaths. NYHA class was significantly improved (p<0.001) and 6 minutes walking distance increased significantly (165.9±102.5m vs. 193.5±115.9m; p=0.007).

Conclusions—Transcatheter treatment of TR with the MitraClip system seems to be safe and feasible in this cohort of preselected patients. Initial efficacy analysis showed encouraging reduction of TR, which may potentially result in improved clinical outcomes.



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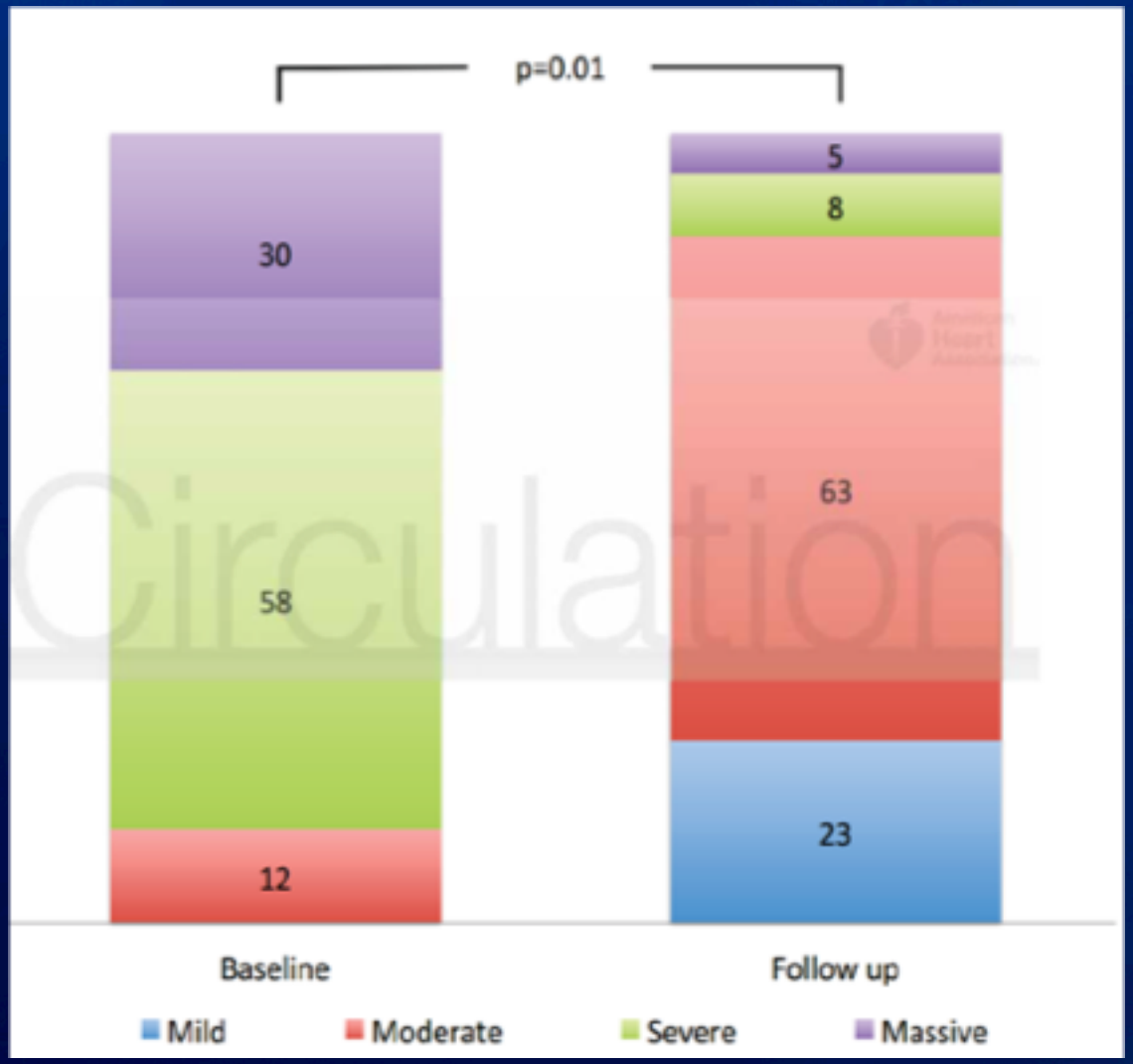
TR Reduction with Clip Implantation



Nickenig G et al. Circulation 2017

Observations

- Transfemoral predominant approach
- TTE imaging required in 25% of patients in whom TEE image quality insufficient
- 78% had clip in anteroseptal commissure
- 1 clip: 48%
- 2-4 clips: 42%
- No clip: 3%

Nickenig G et al. Circulation 2017

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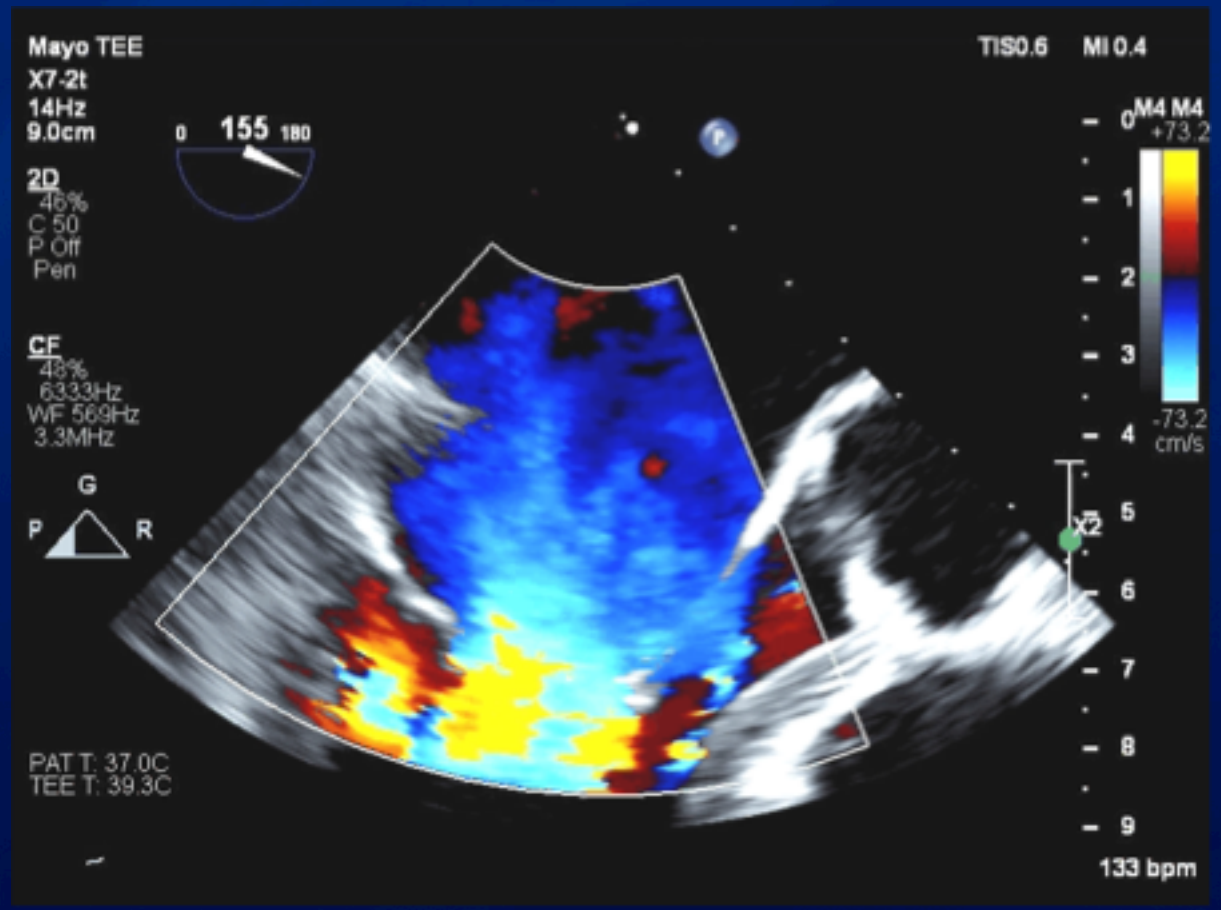
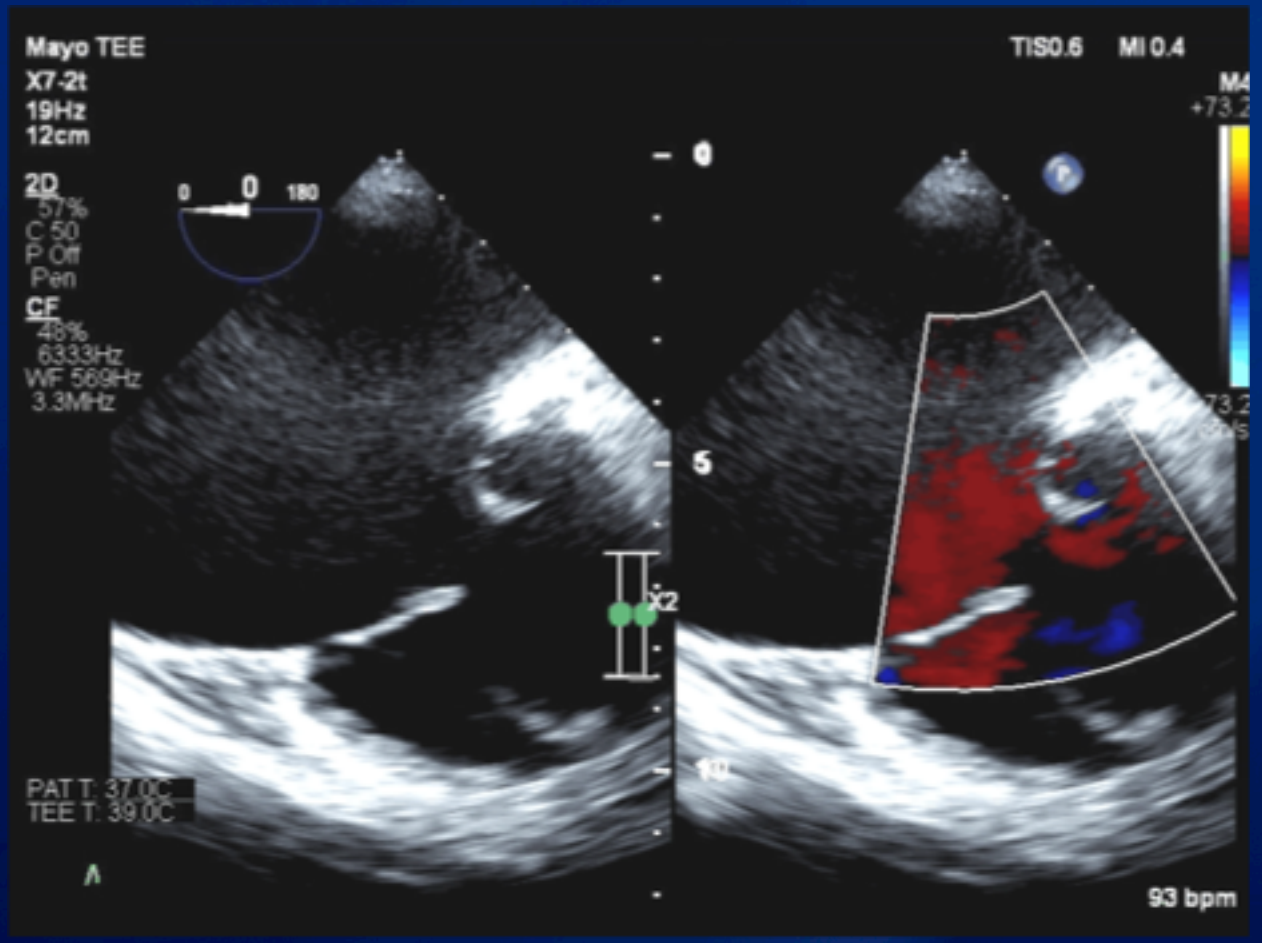
Patient with Severe MR and TR





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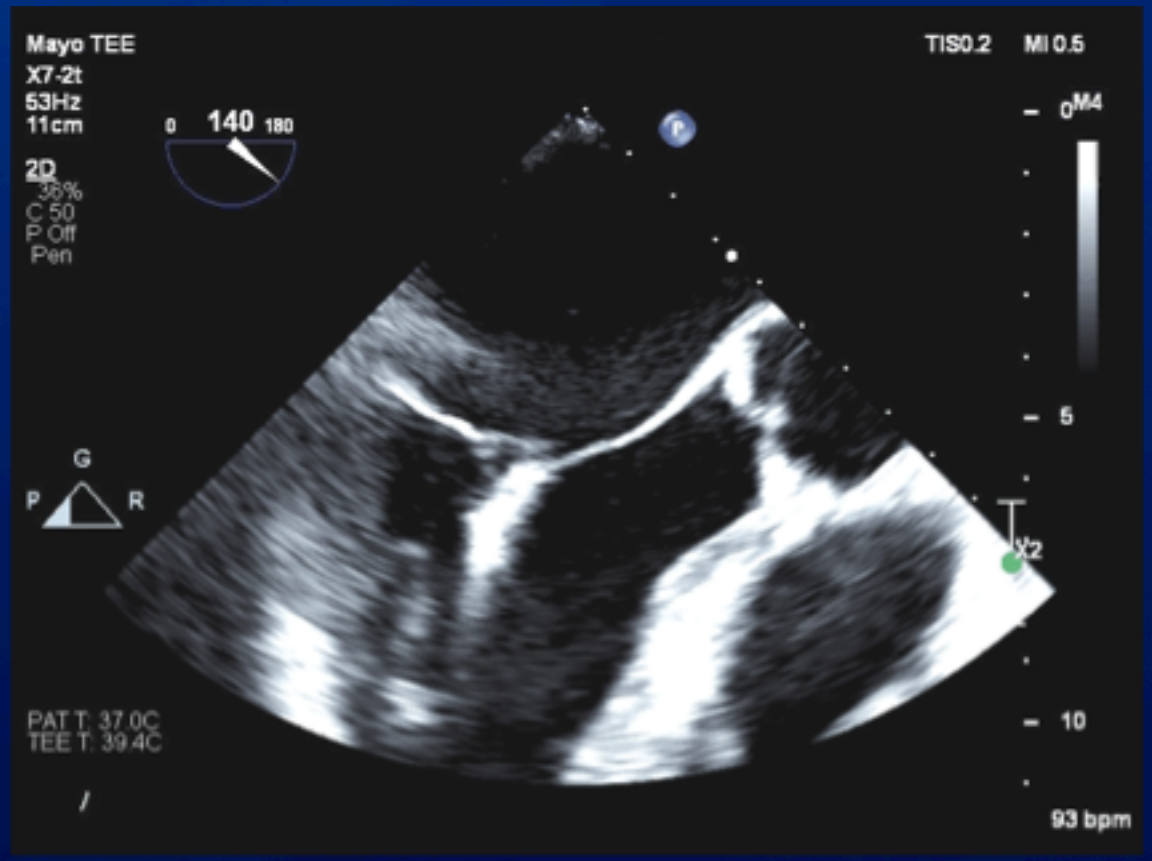
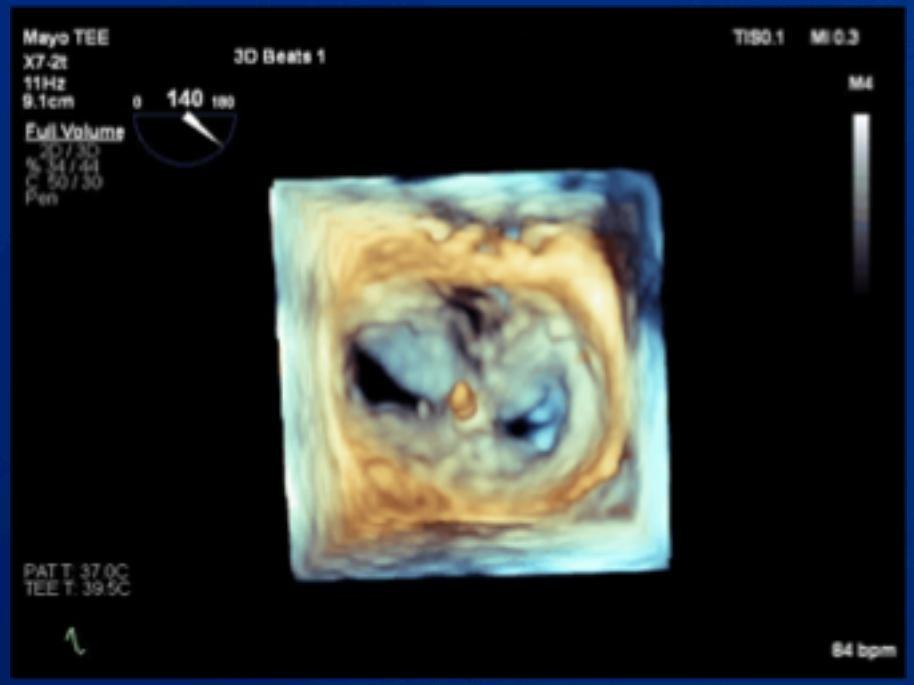
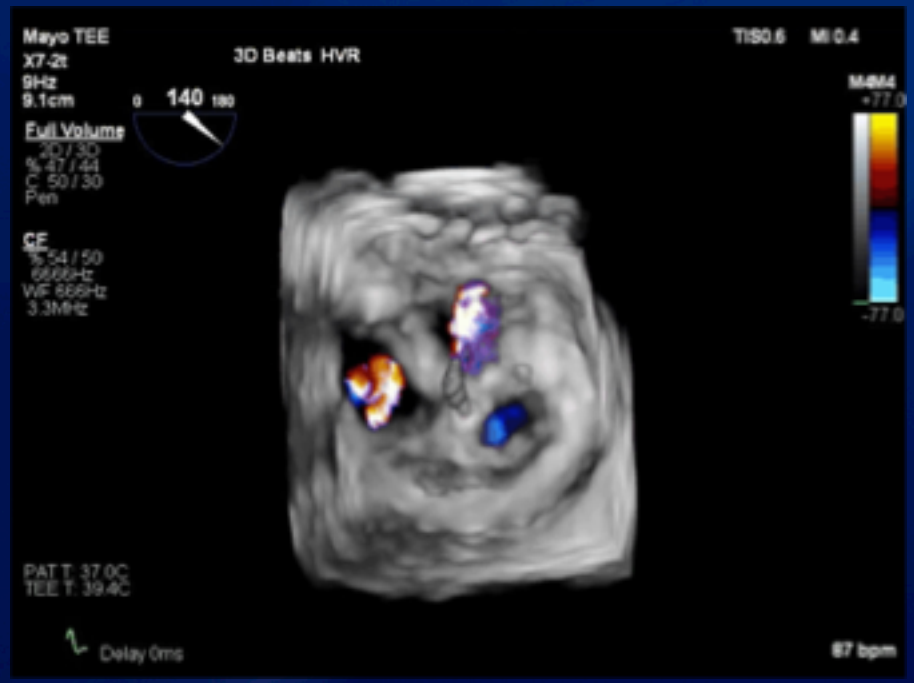
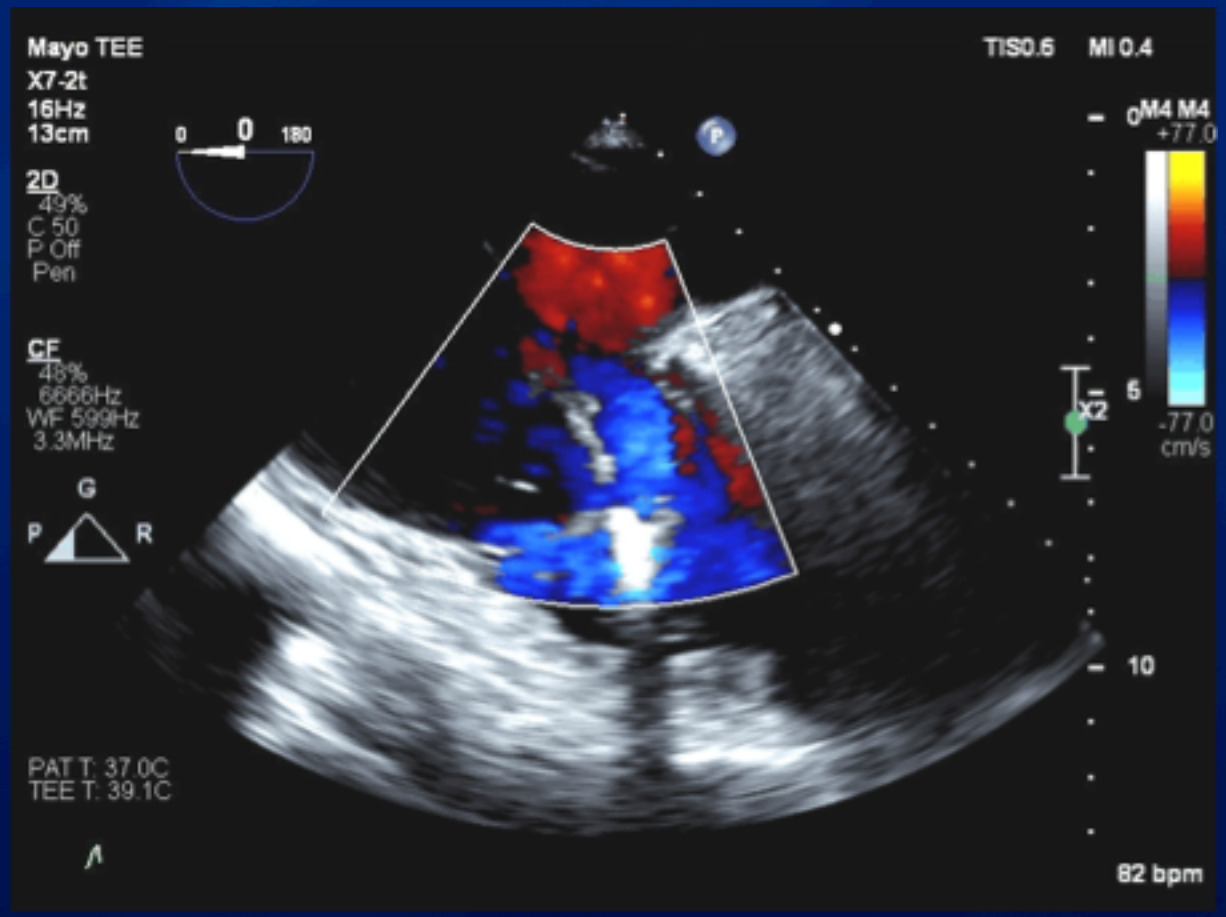
MitraClip Implantation

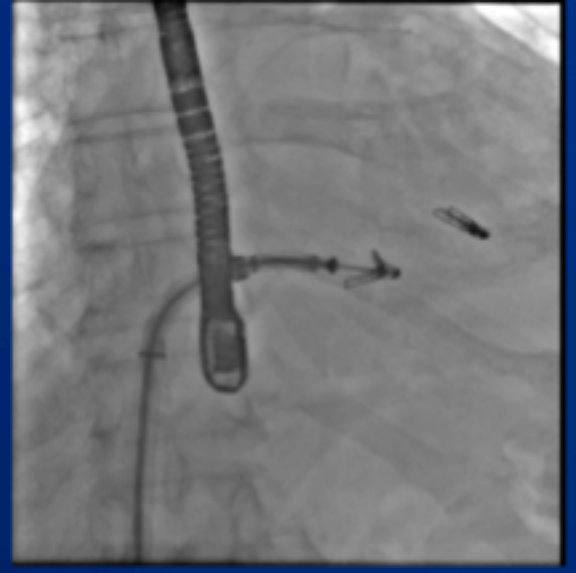


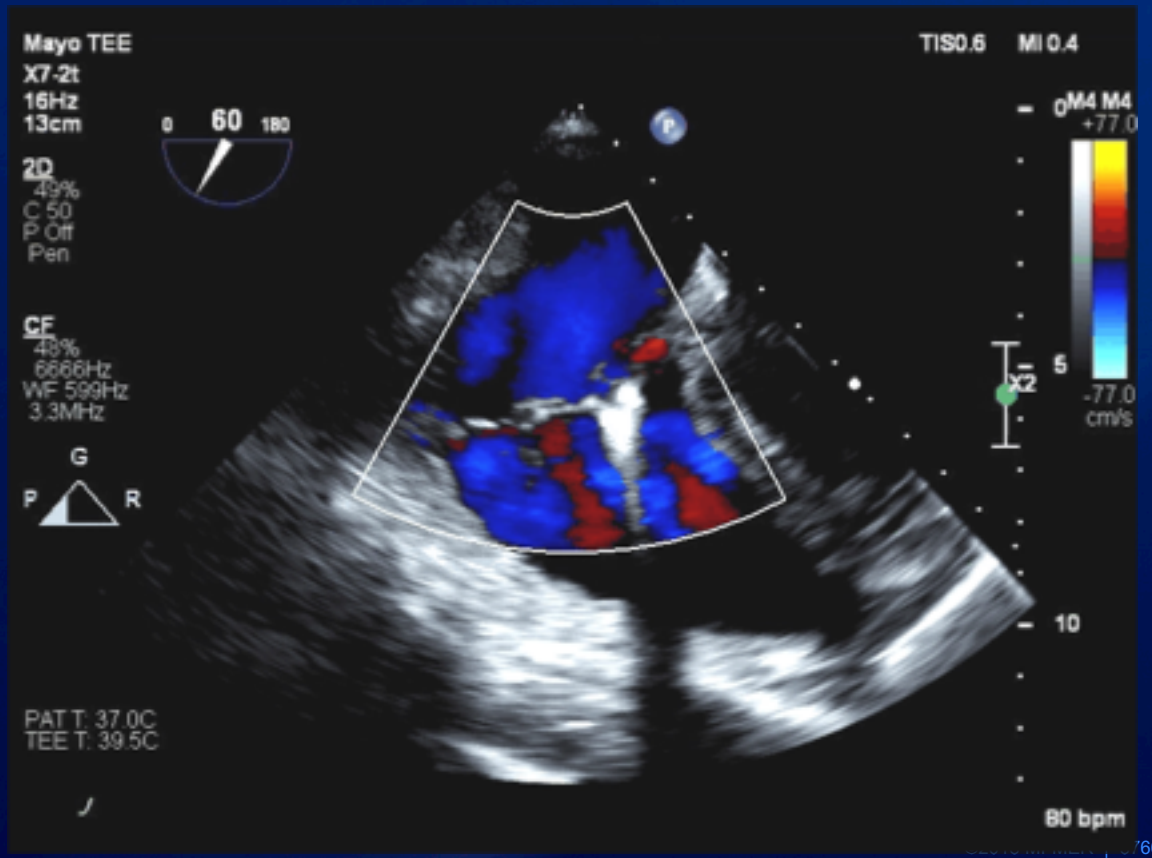




Tricuspid MitraClip Implantation







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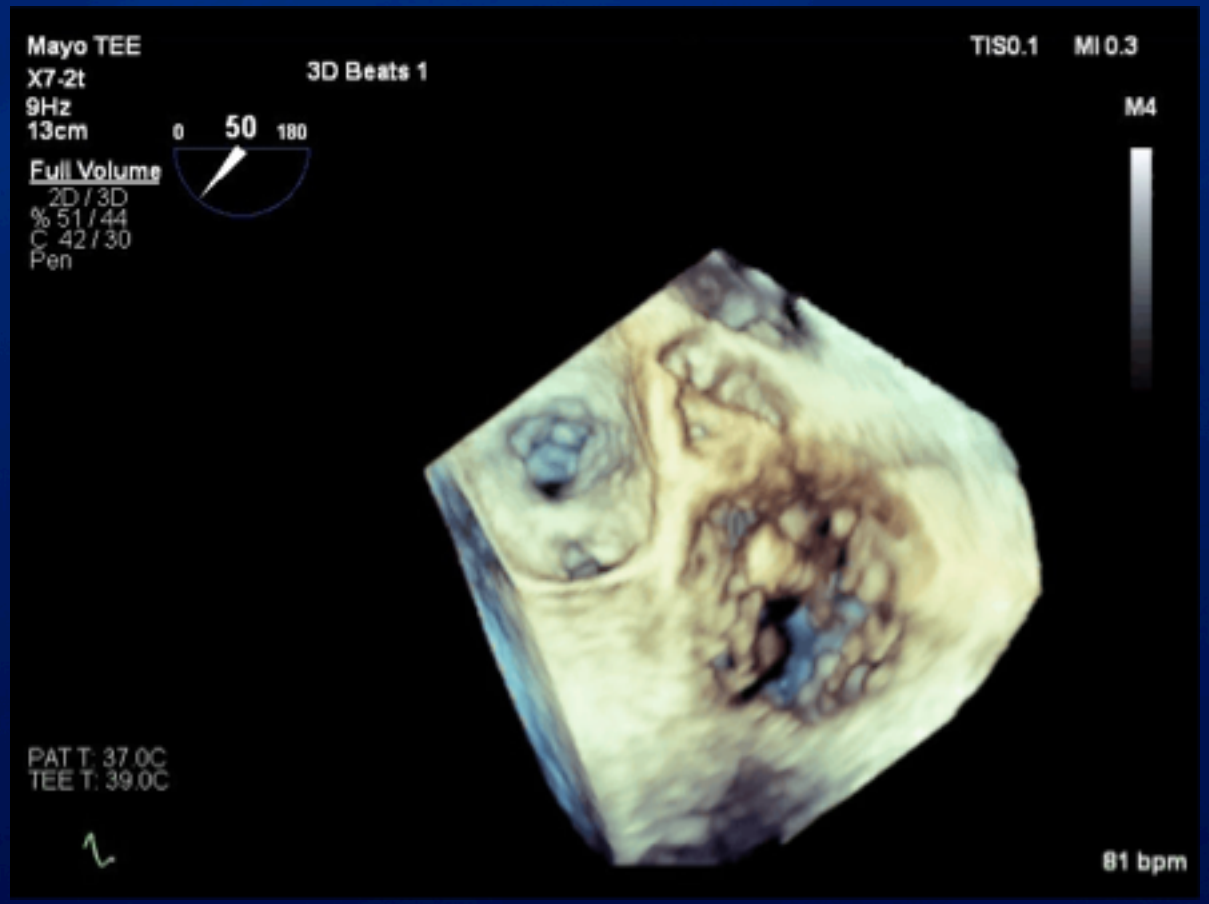
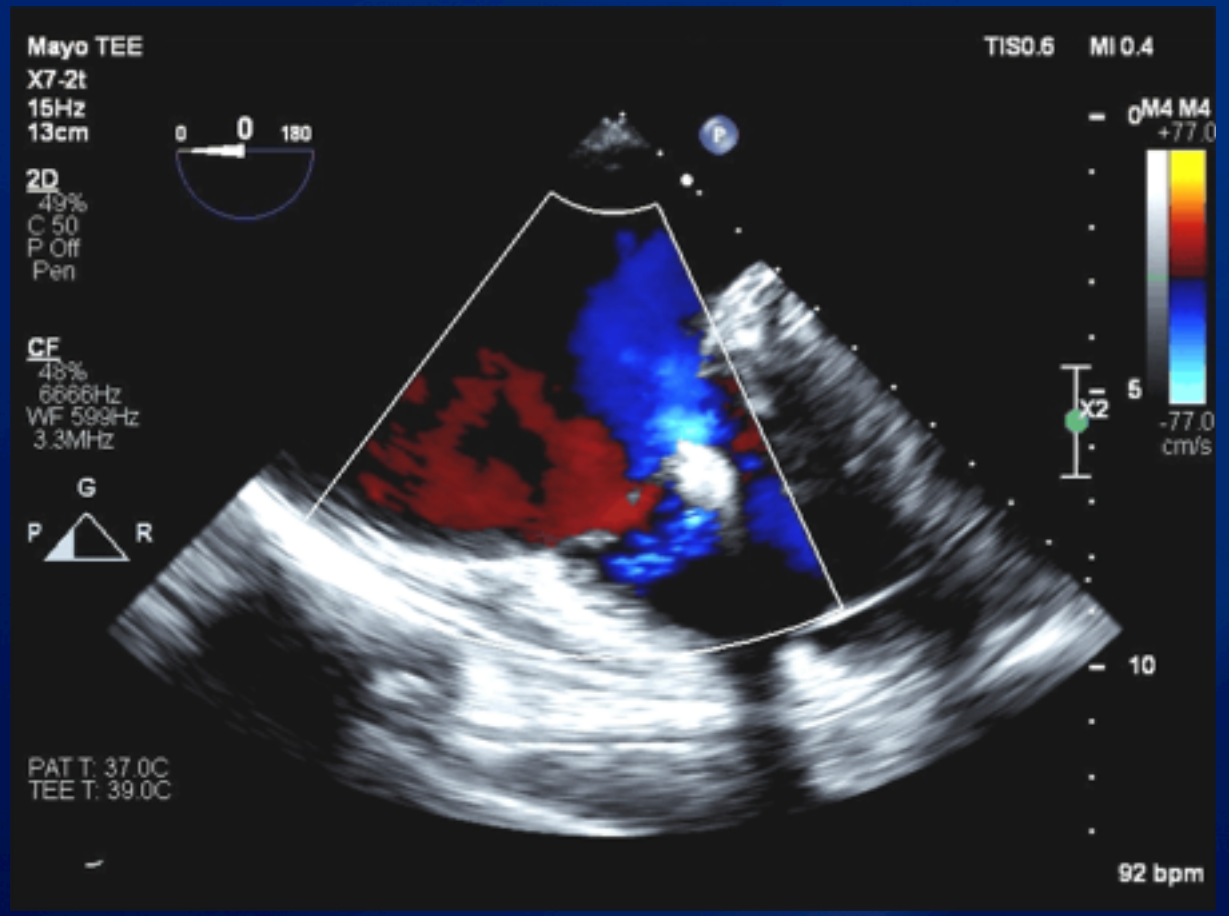
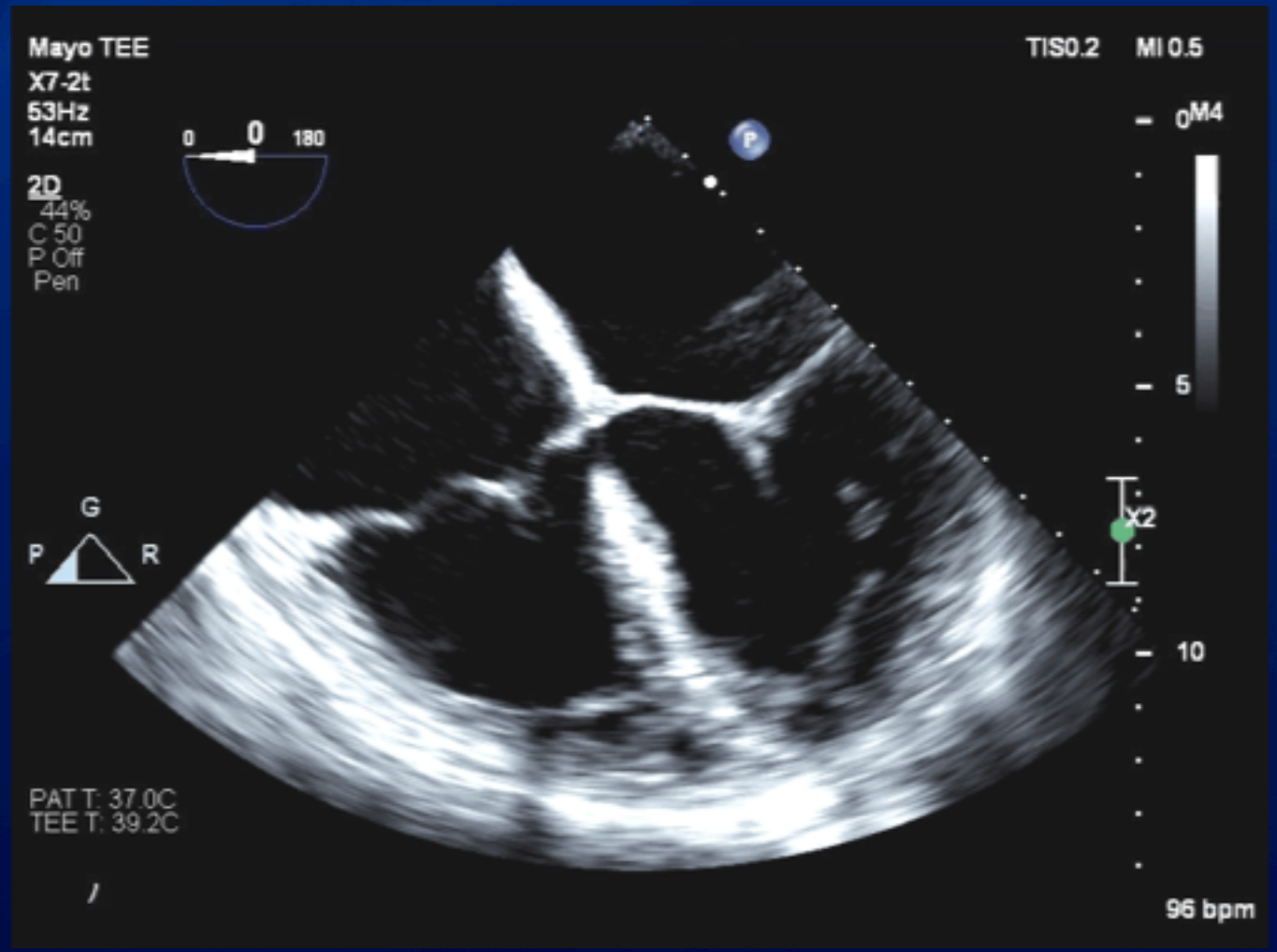
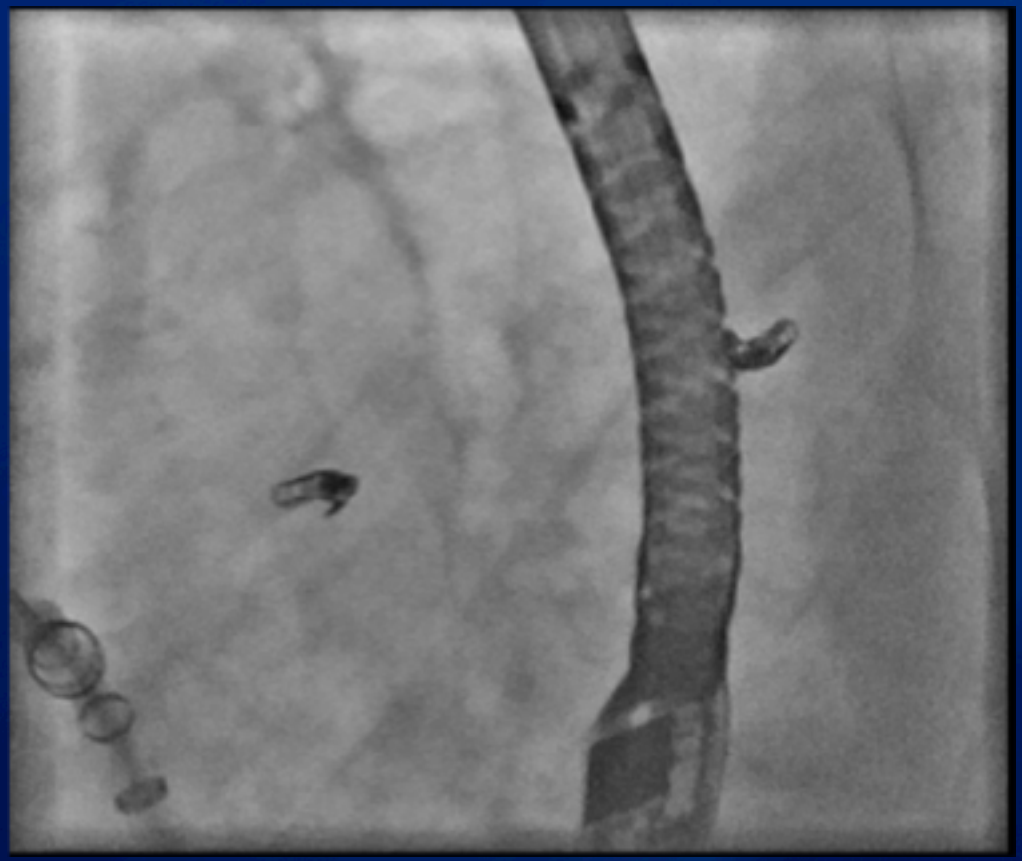
Tricuspid Clip Implantation



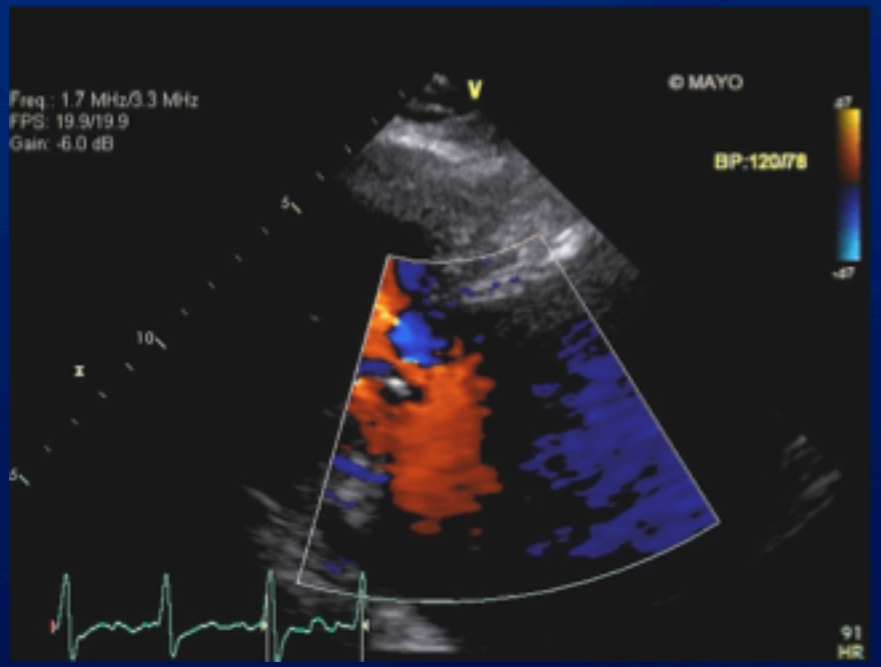


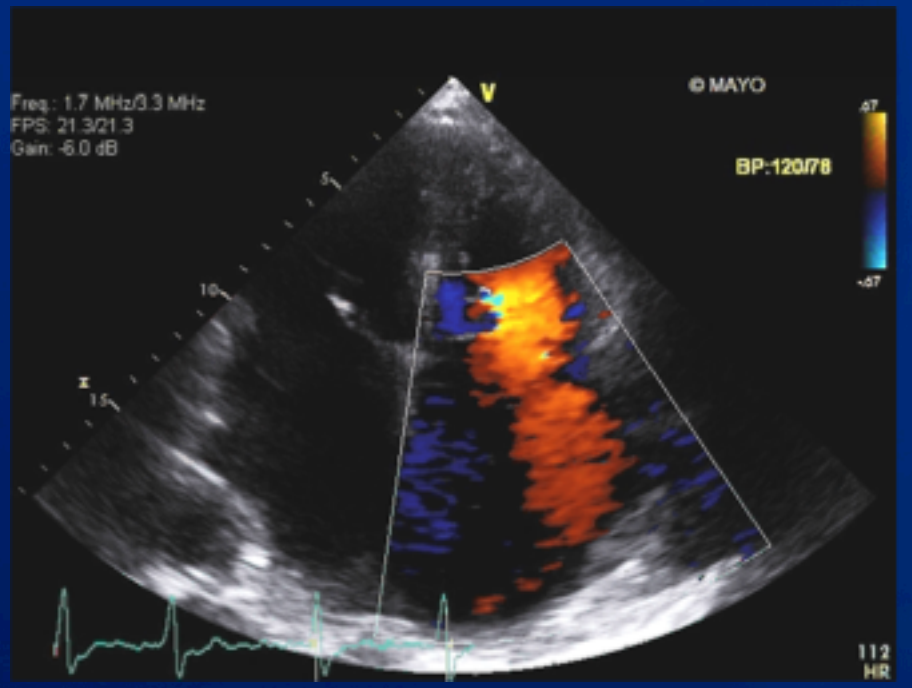
Both Valves Clipped

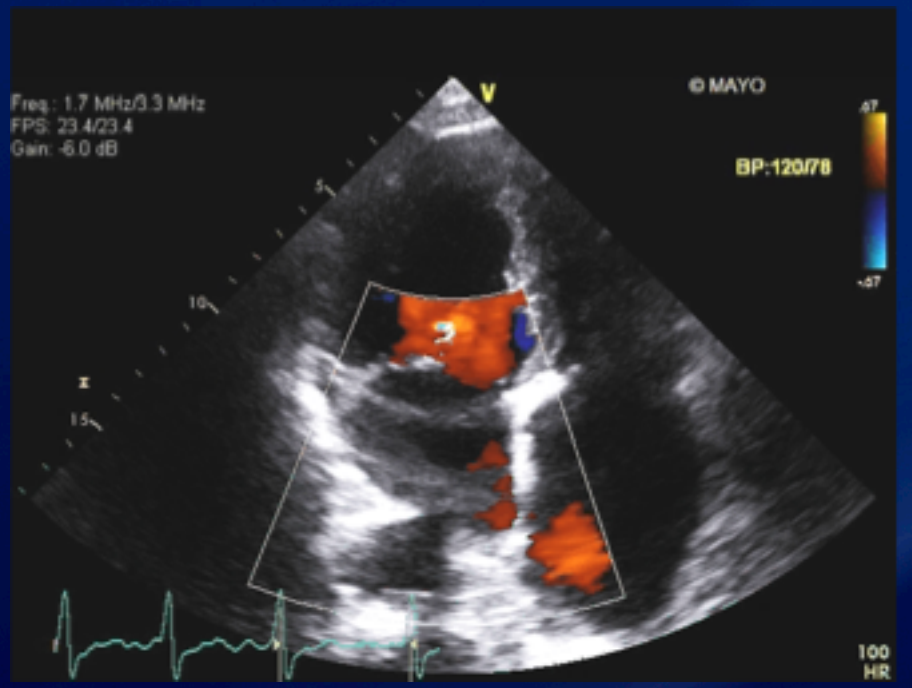




Post-operative Day 1







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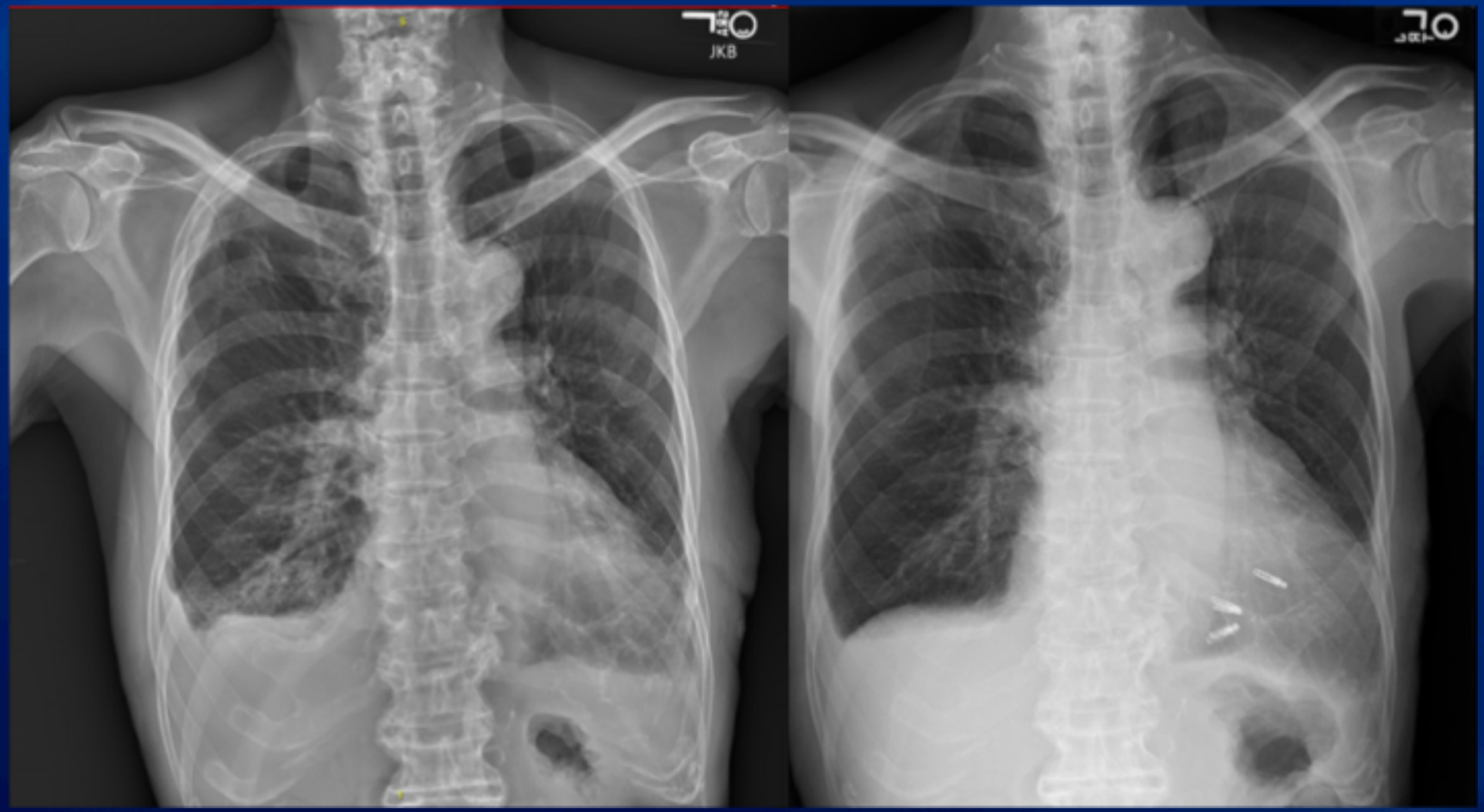
Baseline

30 Day Follow Up



NT pro BNP
2462

NT pro BNP
1676

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Spacer Therapy for TR

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69-Year-Old Female with NYHA Class III Dyspnea

- Abdominal fullness, and lower extremity edema managed with high-dose diuretics
- Previous CABG 15 years prior
- Type 1 Diabetes
- Stage 3 Chronic Kidney Disease
- Paroxysmal atrial fibrillation

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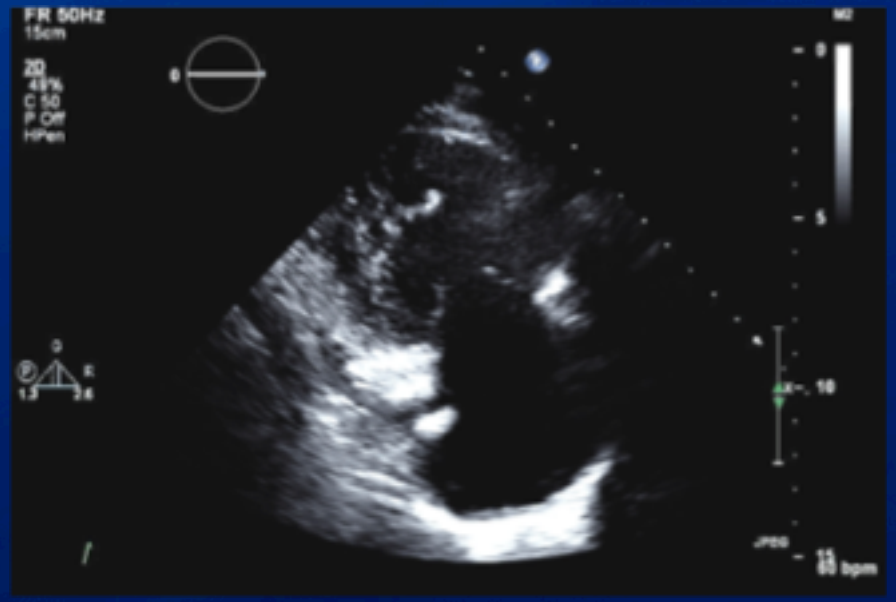
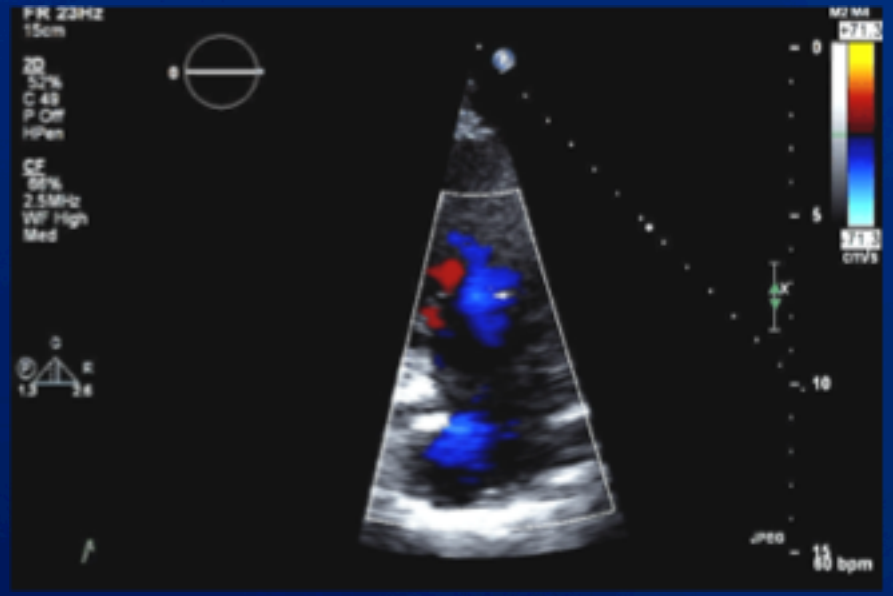
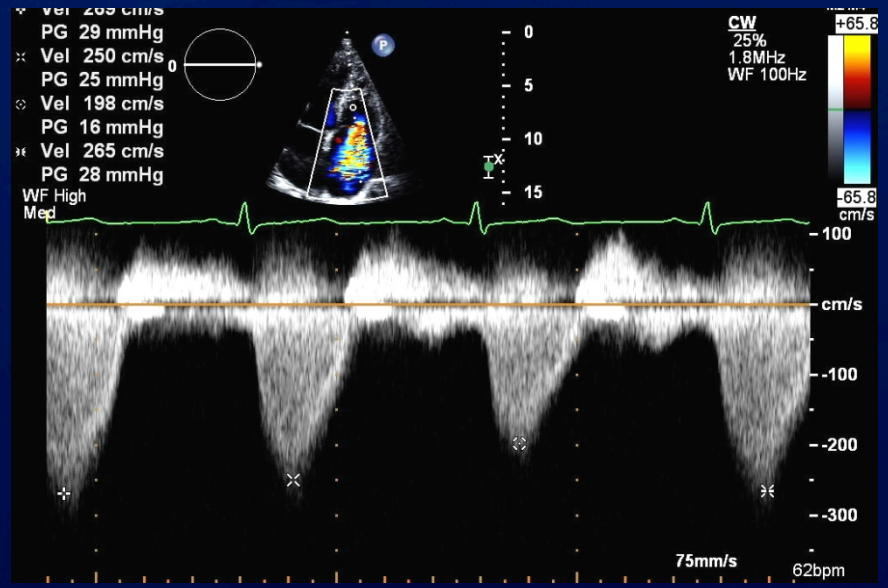
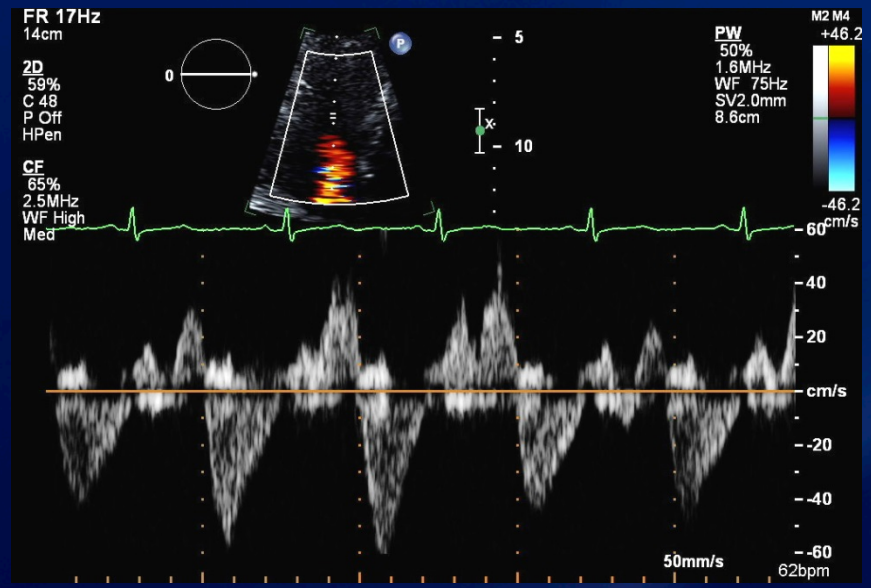
Transthoracic Echocardiogram









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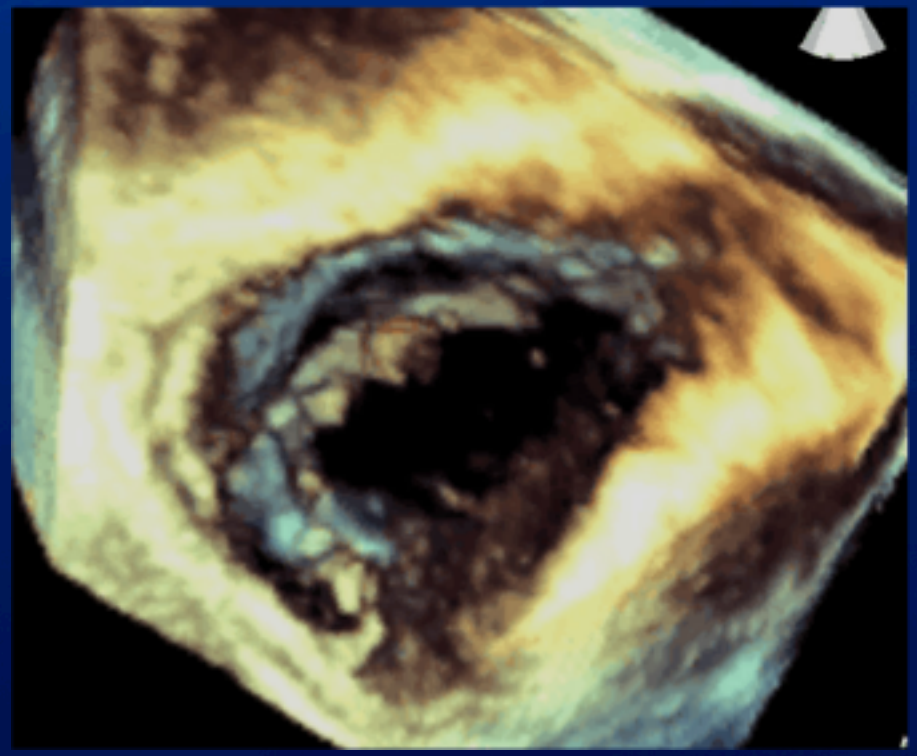
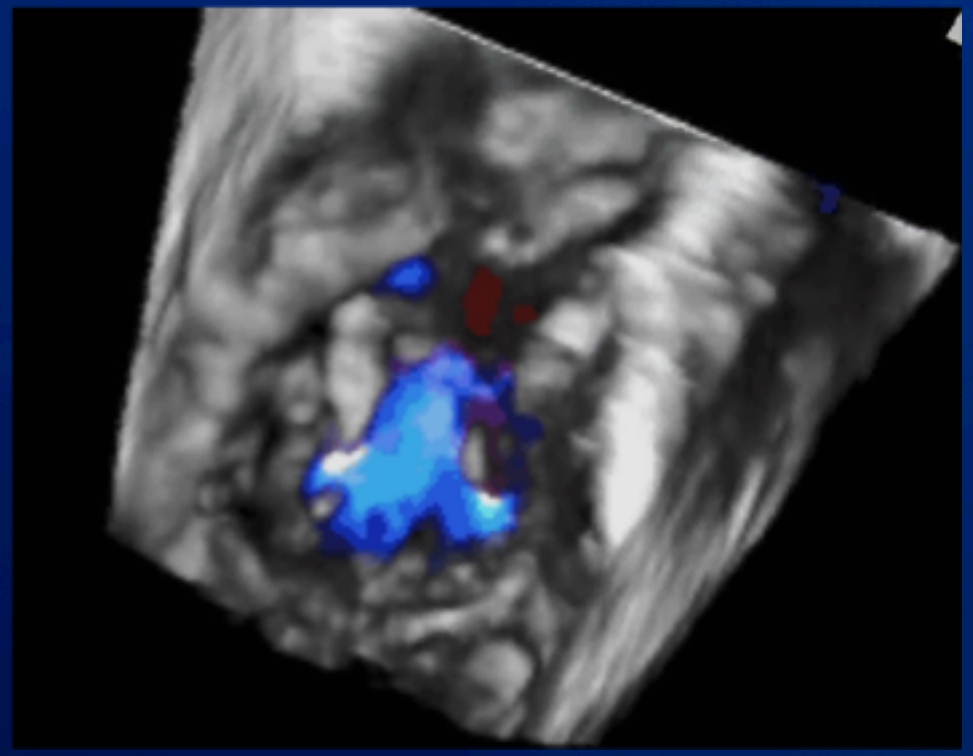
Pre-Procedure

Large Central Coaptation Defect (Ventricular View)





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FORMA Repair System

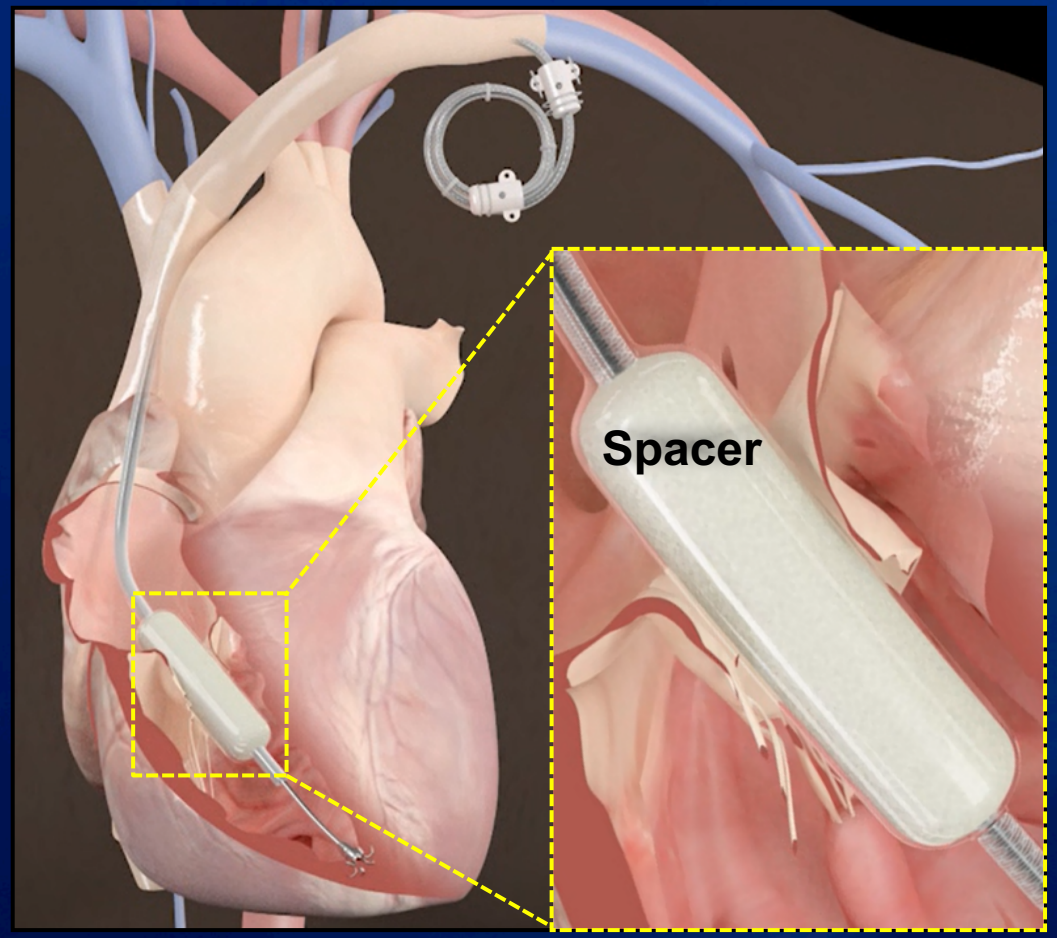
Spacer

- Positioned into the regurgitant orifice
- Creates a platform for native leaflet coaptation

Rail

- Tracks Spacer into position
- Distally and proximally anchored

Coaptation Device Diameter Size	Sheath Size (Fr)
12mm	20
15mm	20
18mm	22



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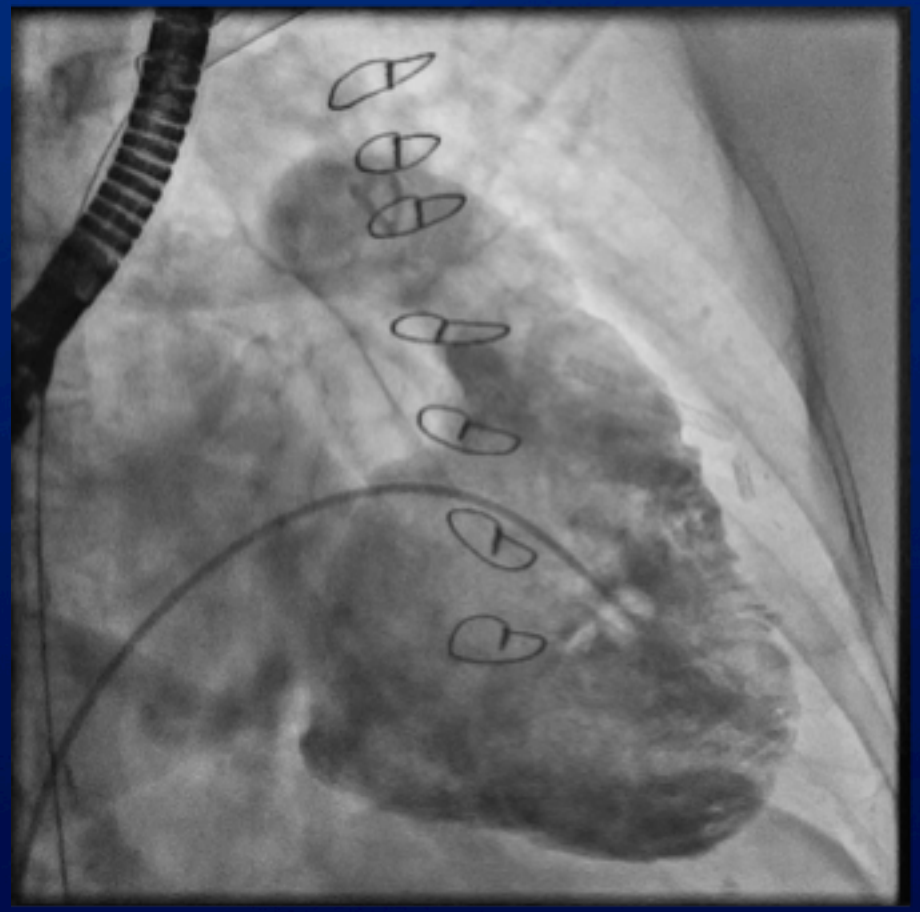
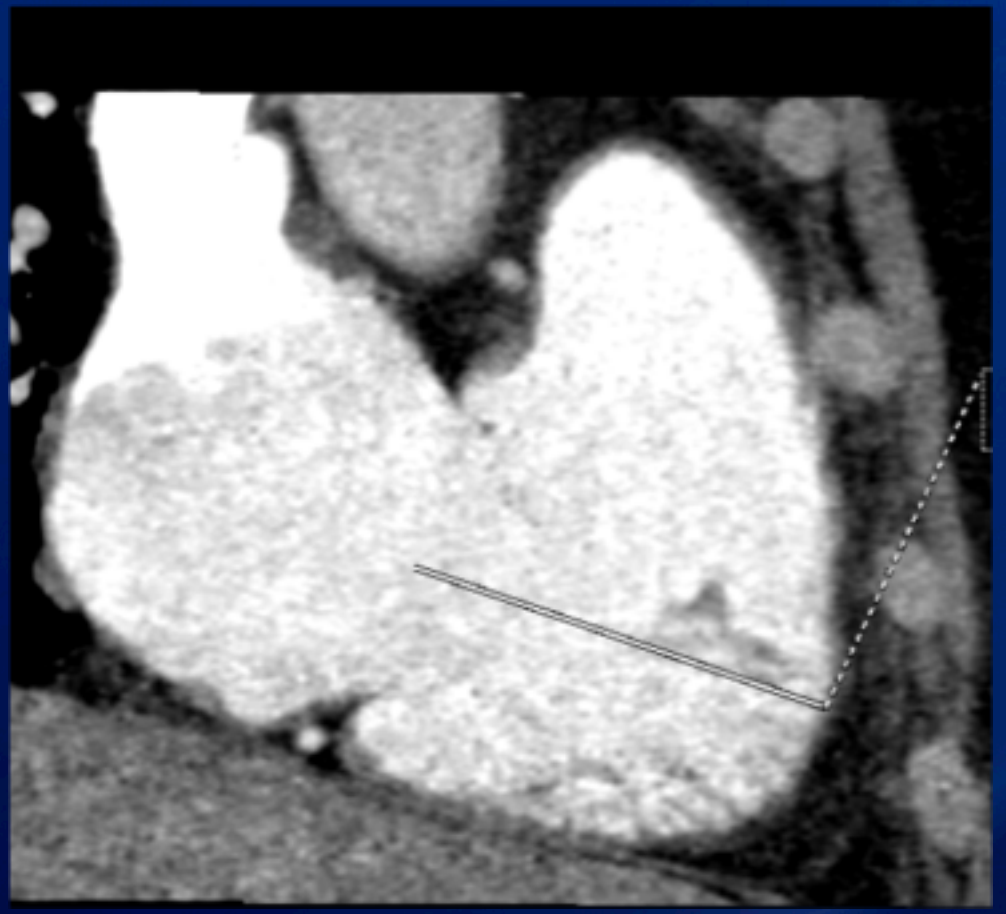
FORMA Procedure





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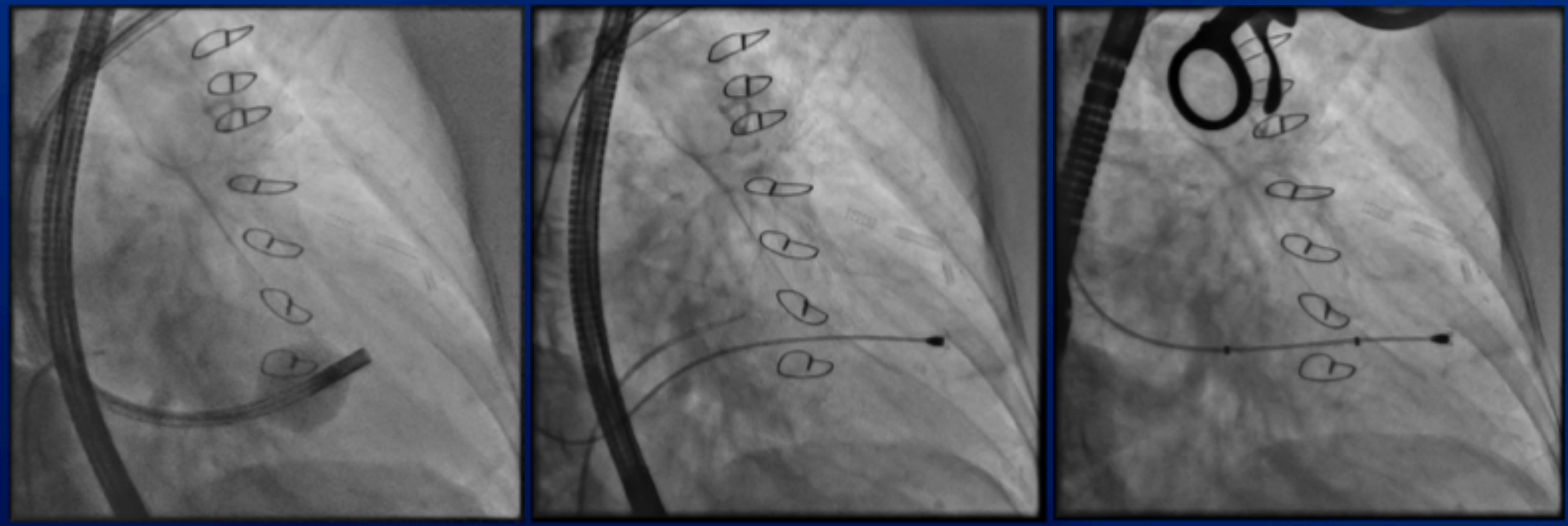
FORMA Procedure



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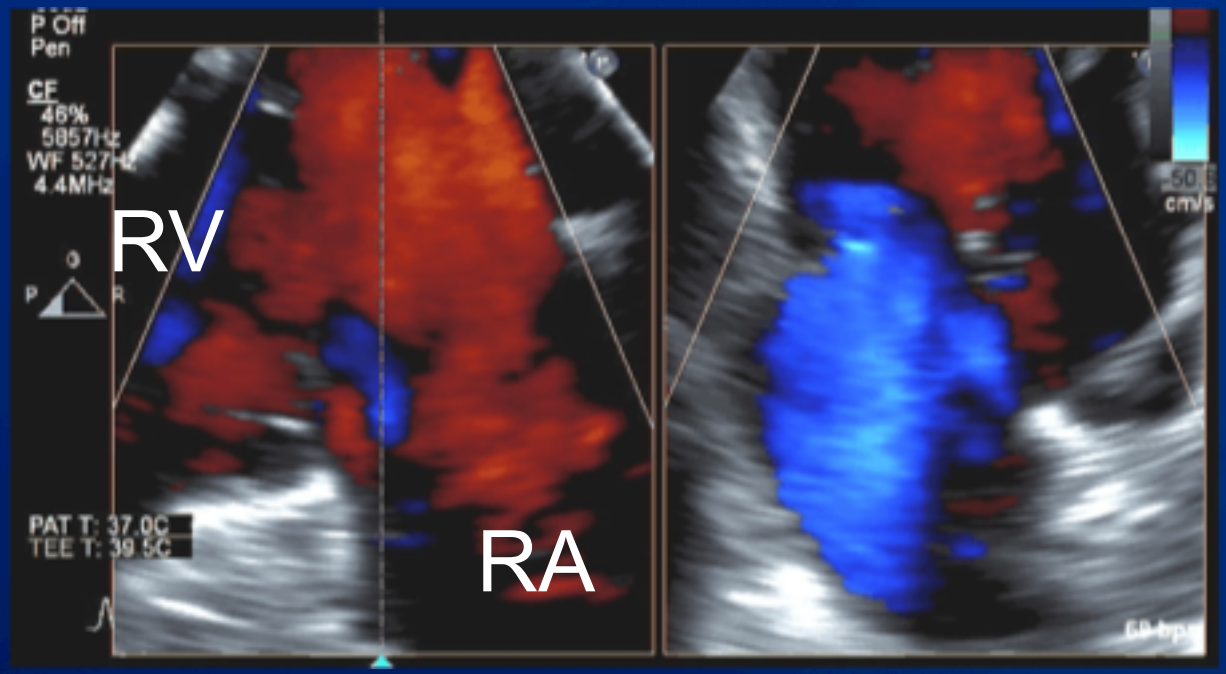
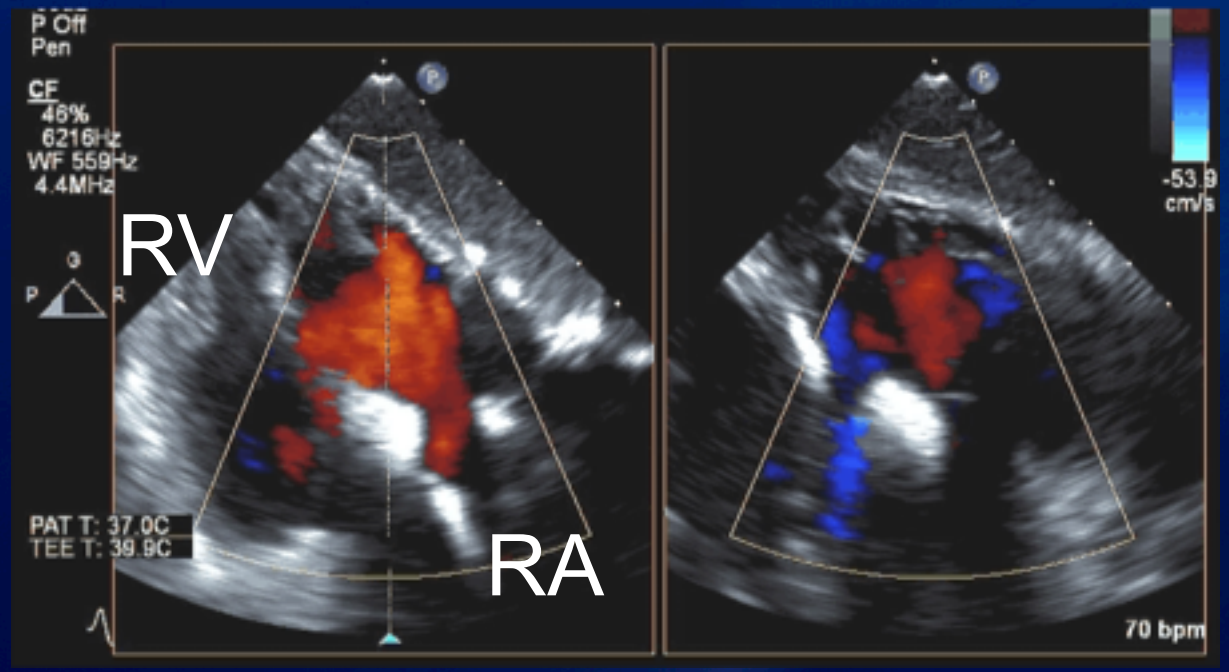
Acute Results

Pre



Post



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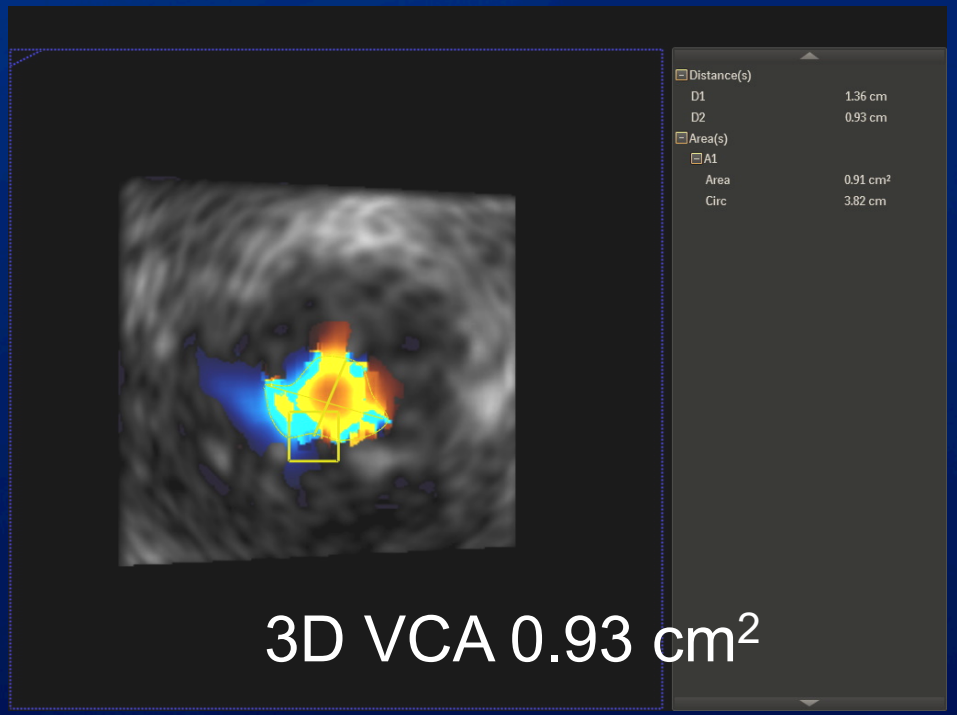
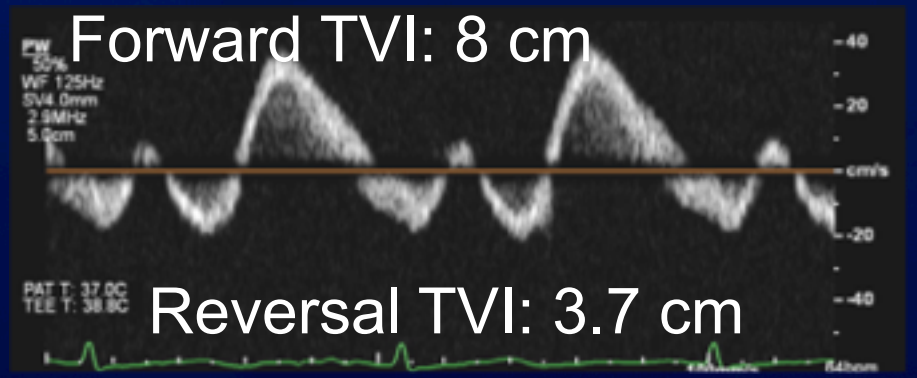
Results: 3D Vena Contracta and Hepatic Veins

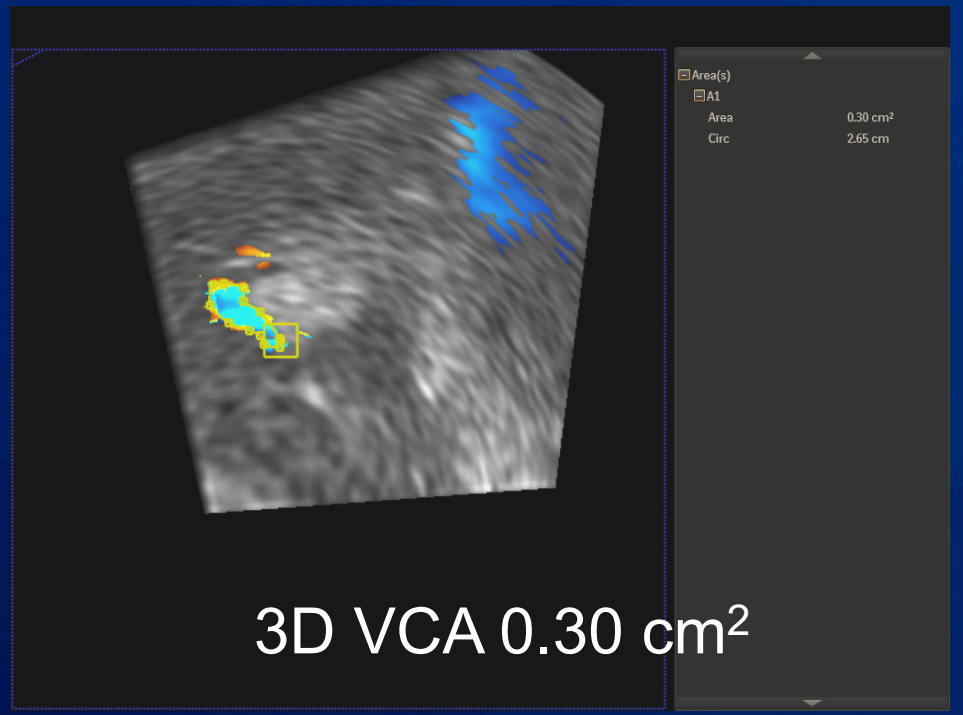
Pre



3D VCA 0.93 cm^2



Post



3D VCA 0.30 cm^2

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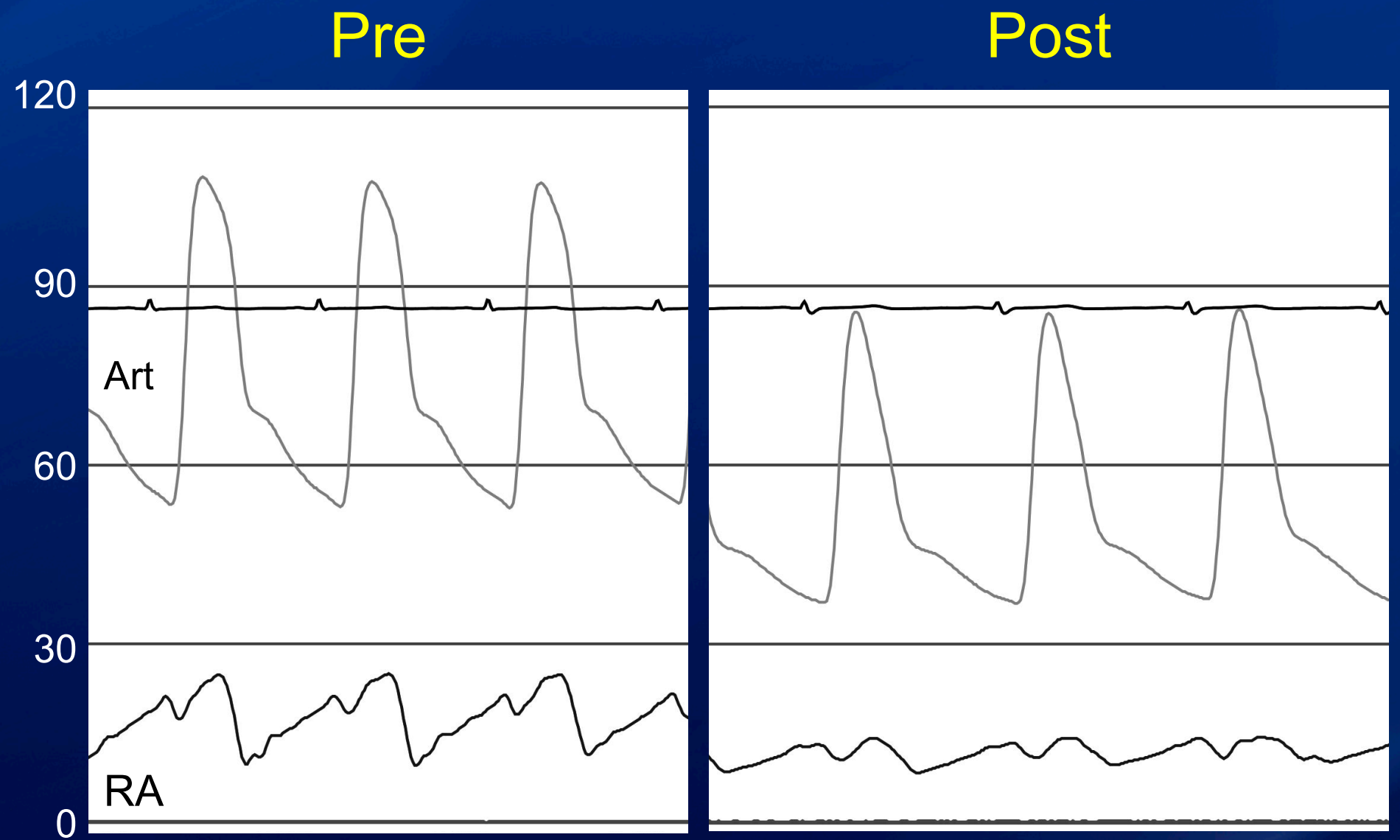

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Follow-up Data

	Baseline	1-Month	6-Months
NYHA Class	3	2	2
6 MW	320 (77%)	384 (95%)	549 (136%)
Edema	2+	Trace	Trace
NT-pro BNP	1,182	415	439
Bilirubin	3.4	2.0	1.7

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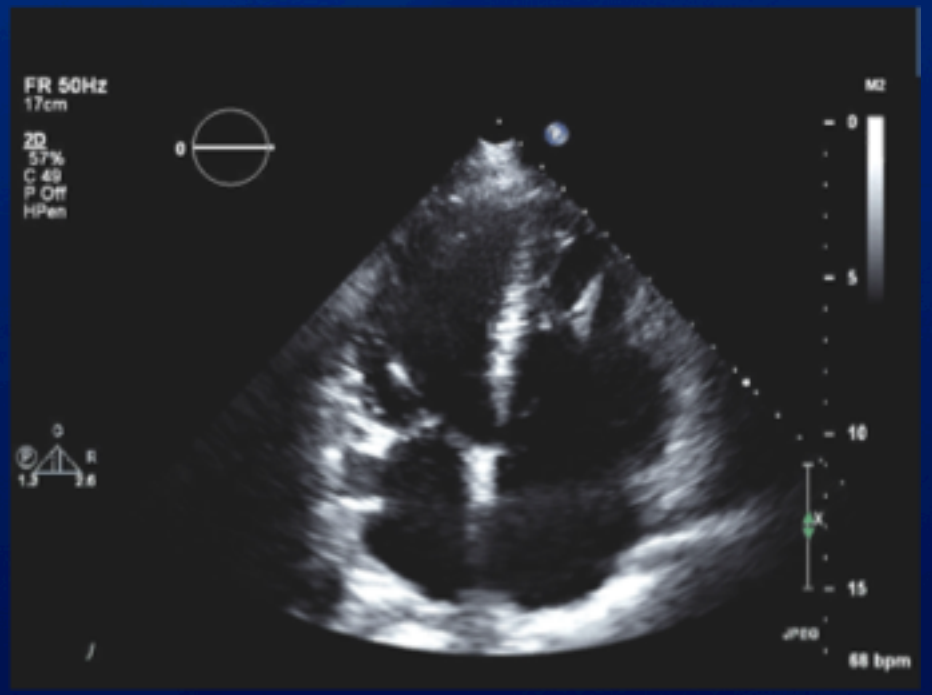
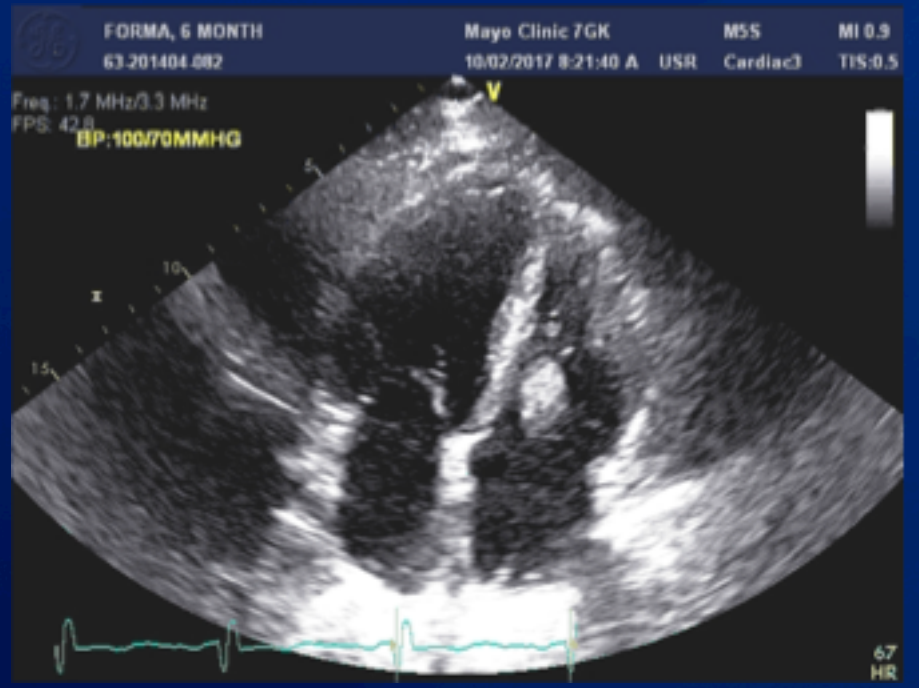
RV and Tricuspid Annulus Changes

Baseline

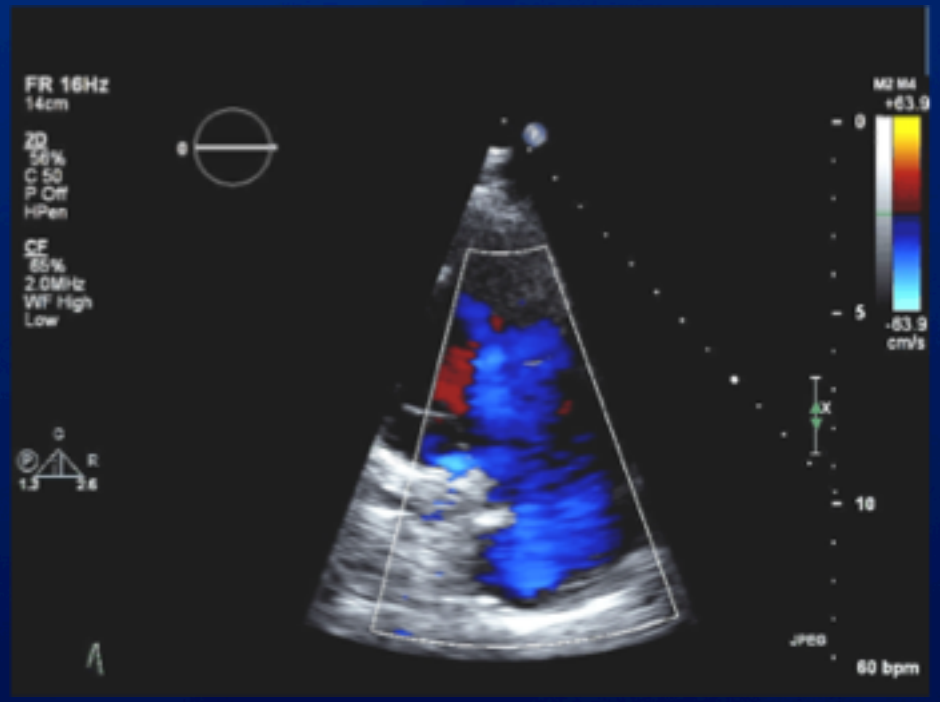


6 Months



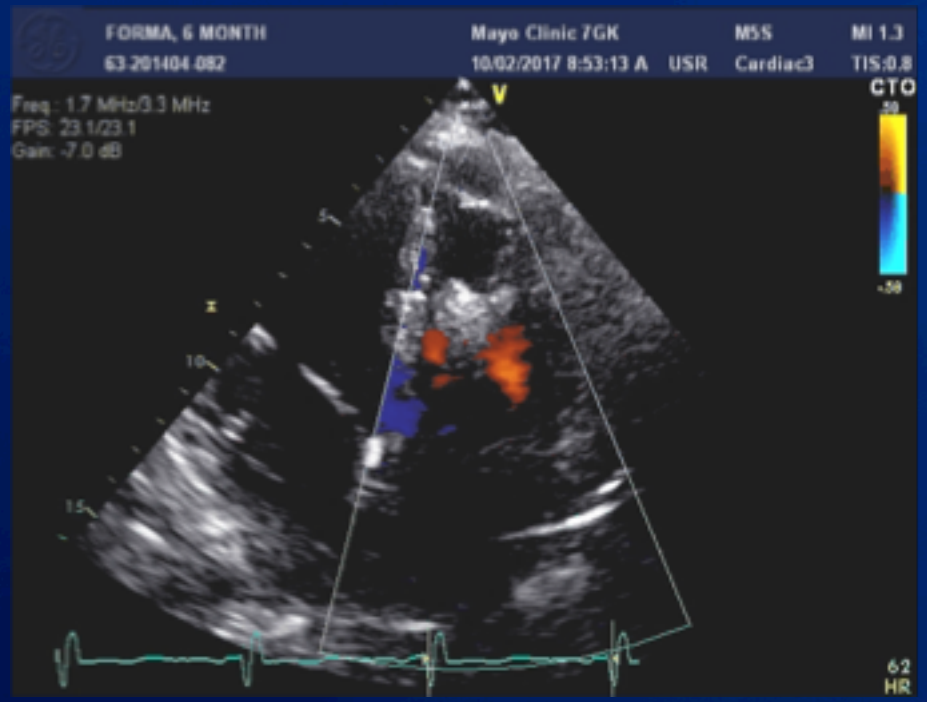
Color Doppler Changes

Baseline



EROA 0.91 cm^2
Reg. Vol. 80 mL

6 Months



EROA 0.5 cm^2
Reg Vol. 46 mL

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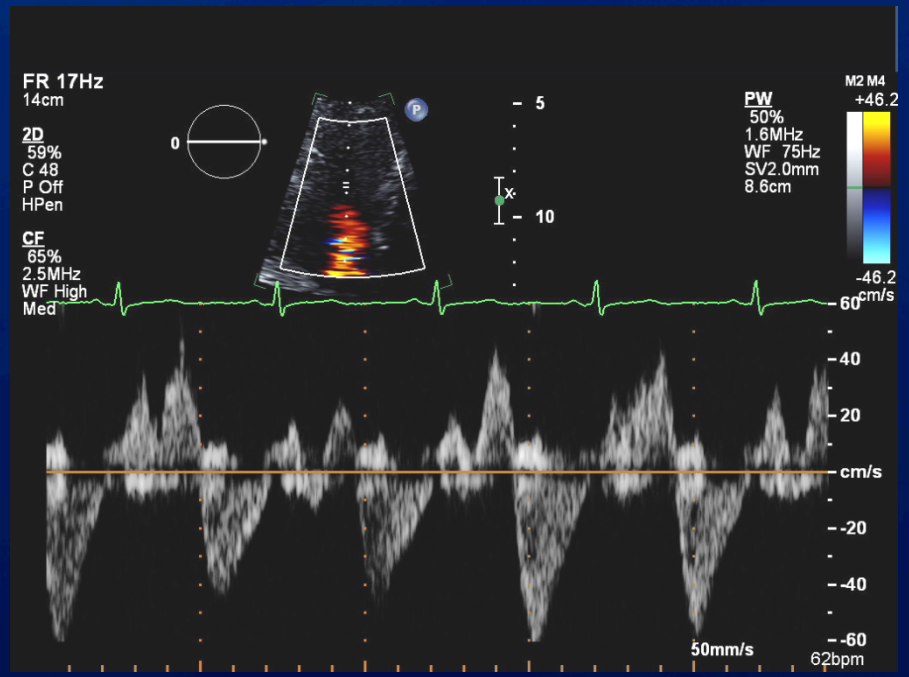
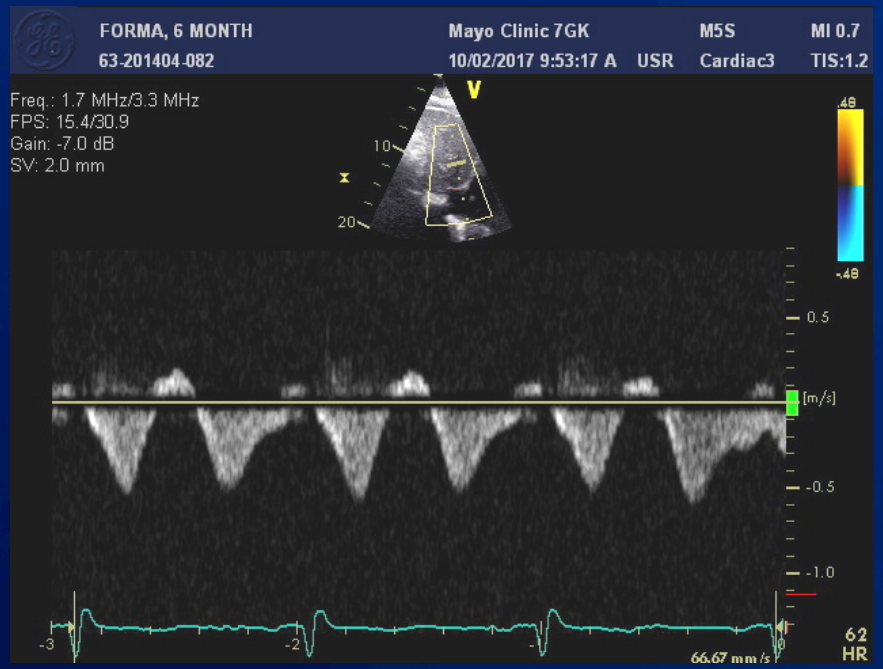
Hepatic Vein Doppler Changes

Baseline



6 Months



FORMA Early Feasibility Study
Participating Sites

Principal Investigator	Hospital	Location
Susheel Kodali, MD	Columbia Medical Center / New York Presbyterian	New York, NY
Vasilis Babaliaros, MD	Emory University Hospital	Atlanta, GA
Raj Makkar, MD	Cedars-Sinai Medical Center	Los Angeles, CA
Mackram Eleid, MD	Mayo Clinic	Rochester, MN
John Brown, MD	Morristown Memorial Hospital	Morristown, NJ

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FORMA Early Feasibility Study
Baseline Characteristics (1)

	Mean or % (n=29)
Age (years)	75.9±8.2
Female Gender	65.5%
Body Mass Index (kg/m^2)	26.3±4.4
NYHA Functional Class III or IV	86%
STS Score[1]	9.1±6.8
EuroSCORE II (%)	8.1±5.3
Serum Creatinine (mg/dl)	1.3±0.4
Atrial Fibrillation	82.8%
Coronary Artery Disease	55.2%
Right Heart Failure	75.9%
Left Heart Failure	17.2%
Diuretic Use	92.9%

[1]Calculated for MVR

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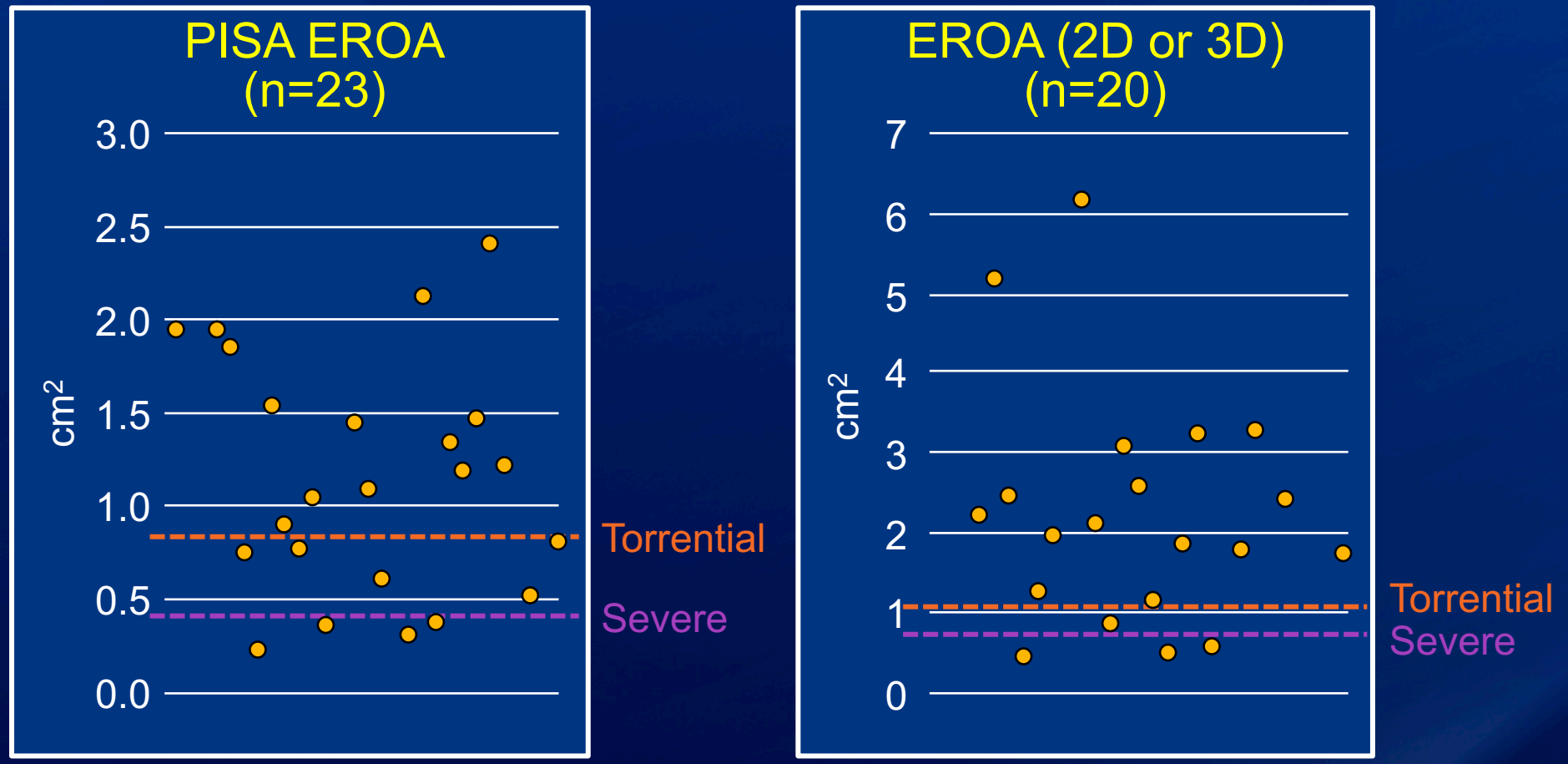
FORMA Early Feasibility Study

Baseline Echocardiography (2)



65% ≥ Torrential TR by PISA EROA; 80% by Quantitative 2D or 3D

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FORMA Early Feasibility Study
Clinical Outcomes at 30 Days

	Patient or % (n=29)
Death (All-Cause)	2 (6.9%)
Stroke/TIA	0 (0.0%)
Vascular Injury	1 (3.4%)
Bleeding*	
Life Threatening or Disabling	2 (6.9%)
Major	4 (13.8%)
Device Related Cardiac Surgery	3 (10.3%)
AKI ≥ Stage 2*	3 (10.3%)

*VARC-2 Guidelines

20/29 patients (69%) had none of the above events

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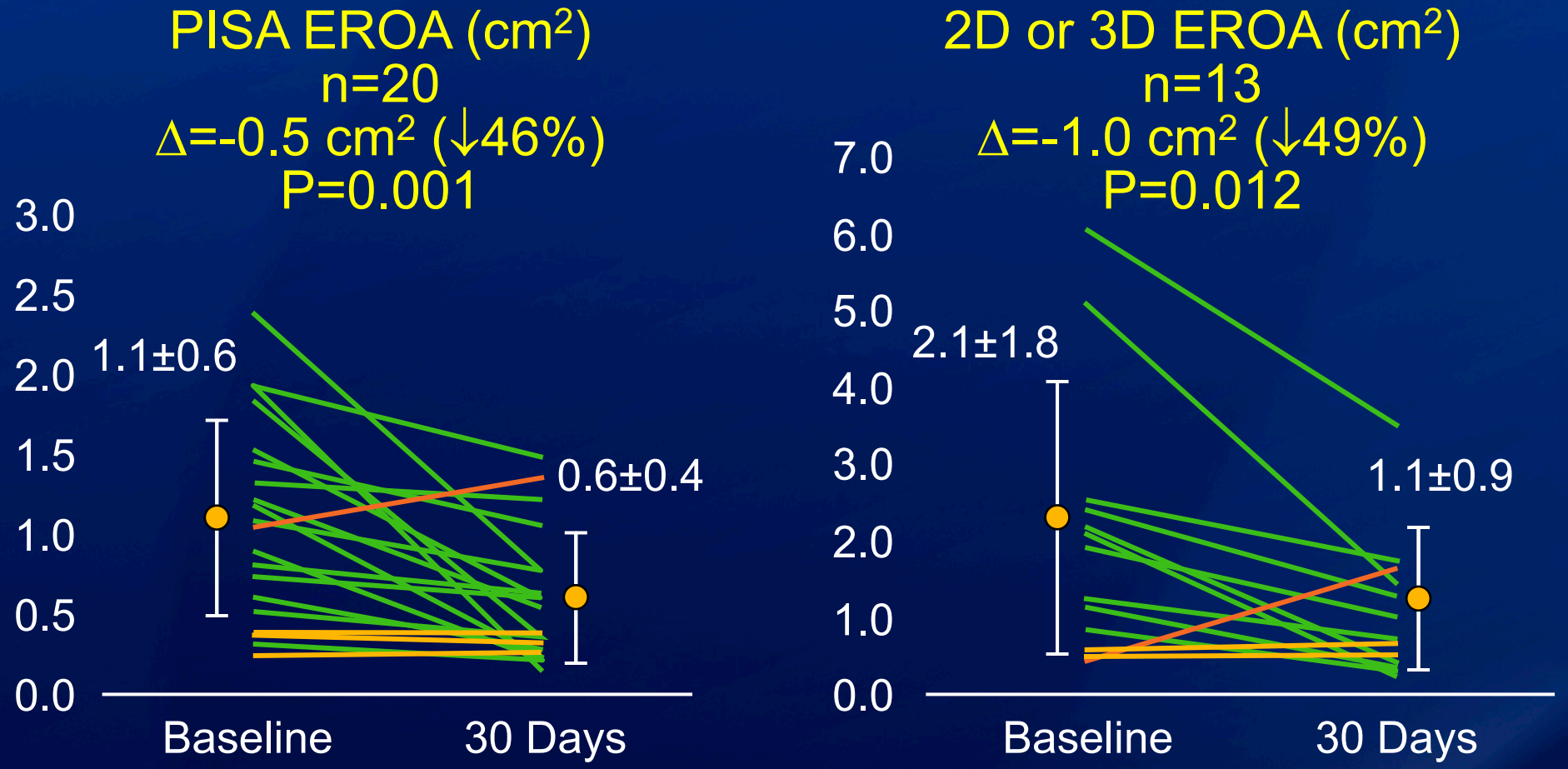
FORMA Early Feasibility Study

Significant Reduction in EROA at 30 Days



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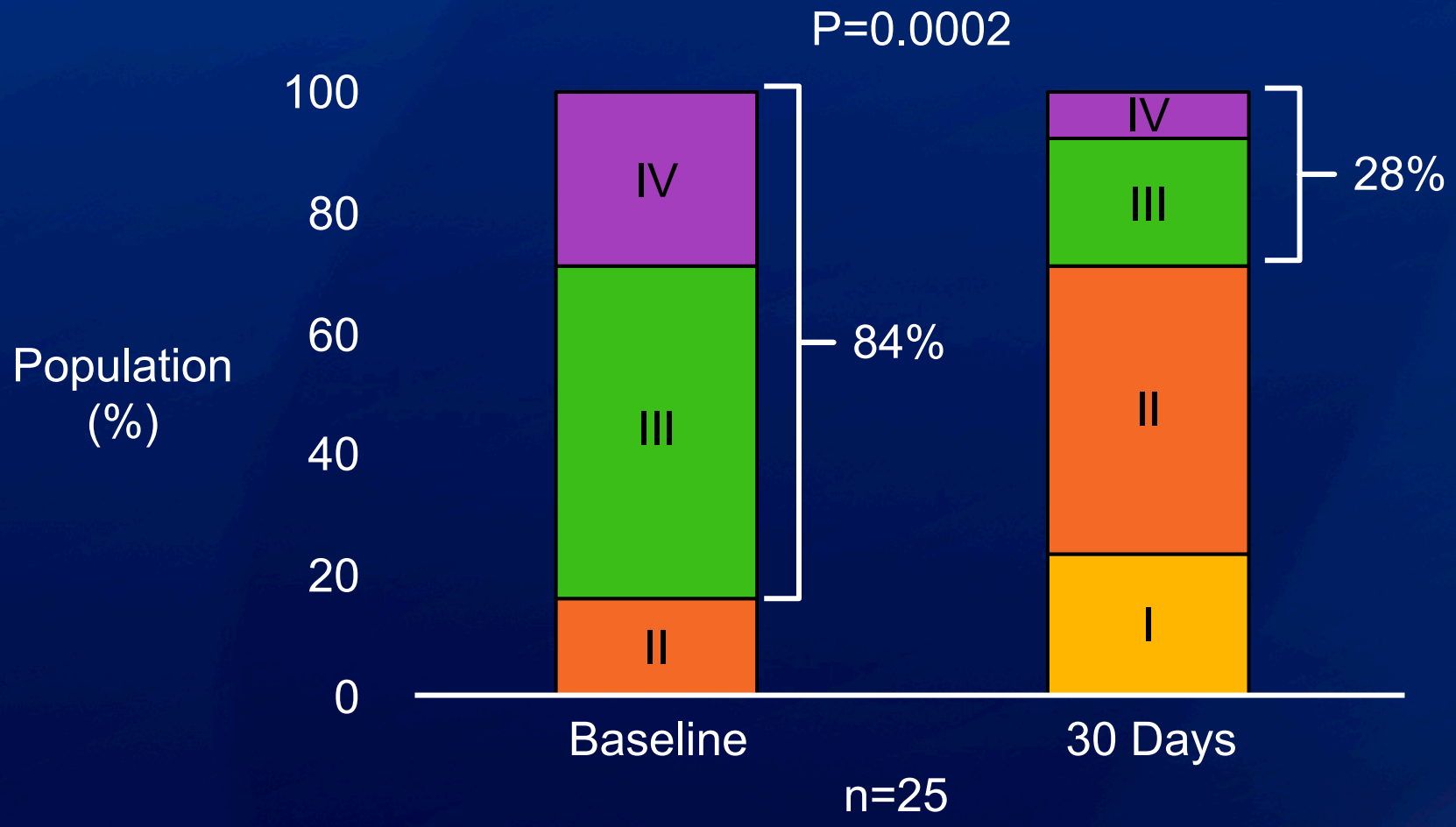
FORMA Early Feasibility Study
Significant Improvement in NYHA Class at 30 Days



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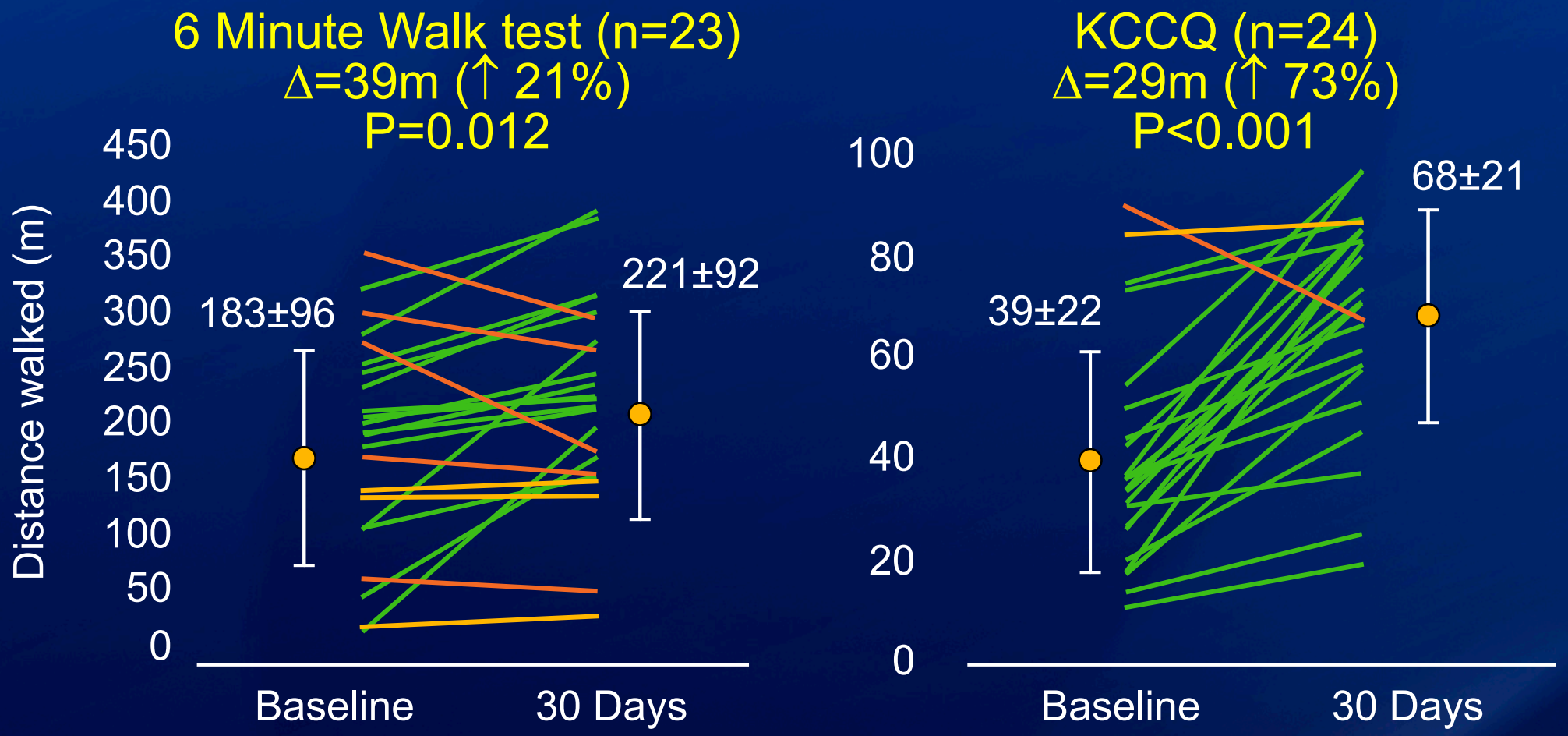
FORMA Early Feasibility Study

Significant Improvement in 6MWT and KCCQ at 30 Days



6MWT – Six Minute Walk Test;
KCCQ-Kansas City Cardiomyopathy Questionnaire Overall Summary Score

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Initial FORMA Compassionate Use 30-Day and 1-Year Clinical Outcomes

	30 day (n=18)	1 year (n=15)
Death	0 (0)	0 (0)
TIA	1 (6)	1 (7)
MI	0 (0)	0 (0)
Rehosp for heart failure	0 (0)	0 (0)
Access-related bleeding		
Life threatening	1 (6)	NA
Major	1 (6)	NA
Minor	2 (11)	NA
Other bleeding events, minor GI	0 (0)	1 (7)

	30 day (n=18)	1 year (n=15)
Vascular complications		
Major	0 (0)	NA
Minor	1 (6)	NA
Hospital stay (days)	4 (2-5)	NA
Acute kidney injury ≥2	0 (0)	1 (7)
Sustained ventricular arrhythmia	0 (0)	0 (0)
Pulmonary embolism	0 (0)	0 (0)
New pacemaker	0 (0)	0 (0)
Device thrombosis	0 (0)	1 (7)
Infection	1 (6)	4 (27)

Perlman G et al: JACC: Cardiovascular Interventions 10:1994, 2017

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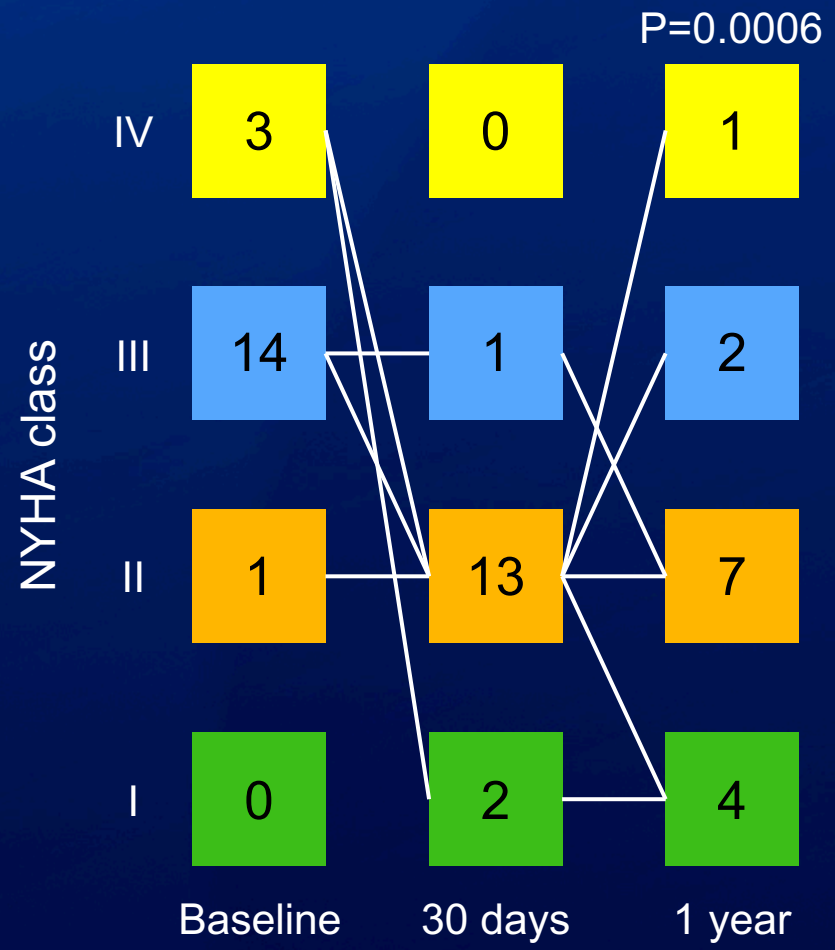
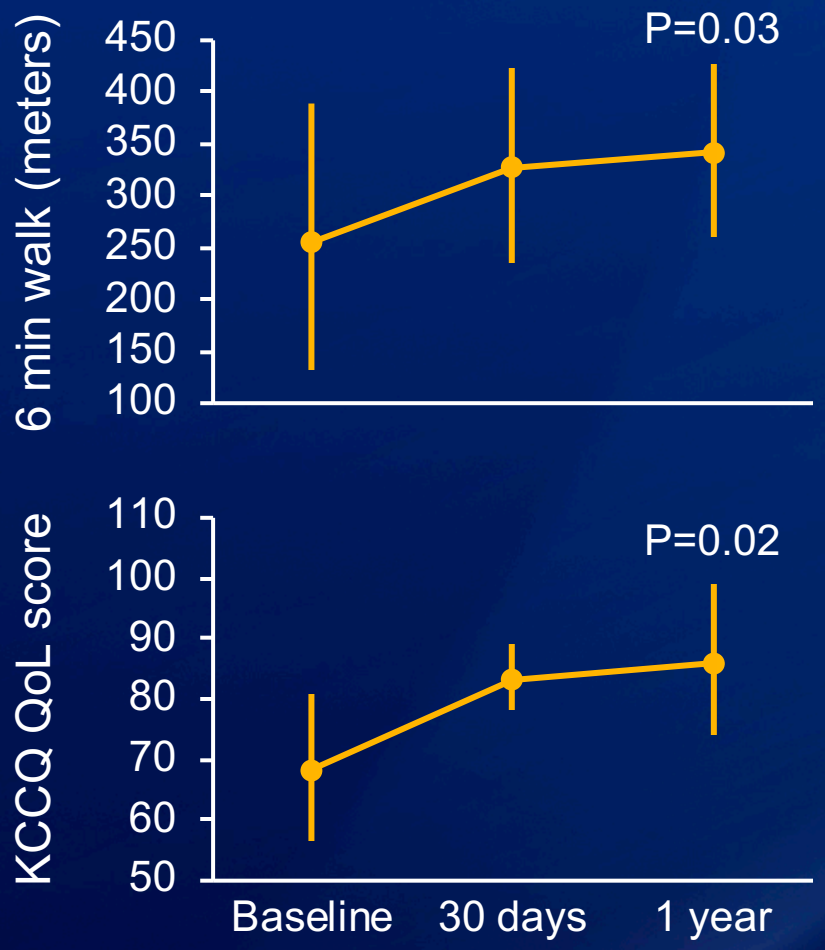
Functional Status After FORMA System Implantation





Perlman G et al: JACC: Cardiovascular Interventions 10:1994, 2017

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Spacer Therapy Conclusions

In a patient cohort with torrential TR and multiple co-morbidities…

- The FORMA Tricuspid Valve Repair System was feasible and the next generation will be introduced soon.
- Despite ‘torrential’ TR in most patients, there was significant reduction of TR (EROA), especially in patients with the most severe TR.
- At 30 days, there was significant improvement in NYHA functional class, 6 minute walk tests and KCCQ scores.

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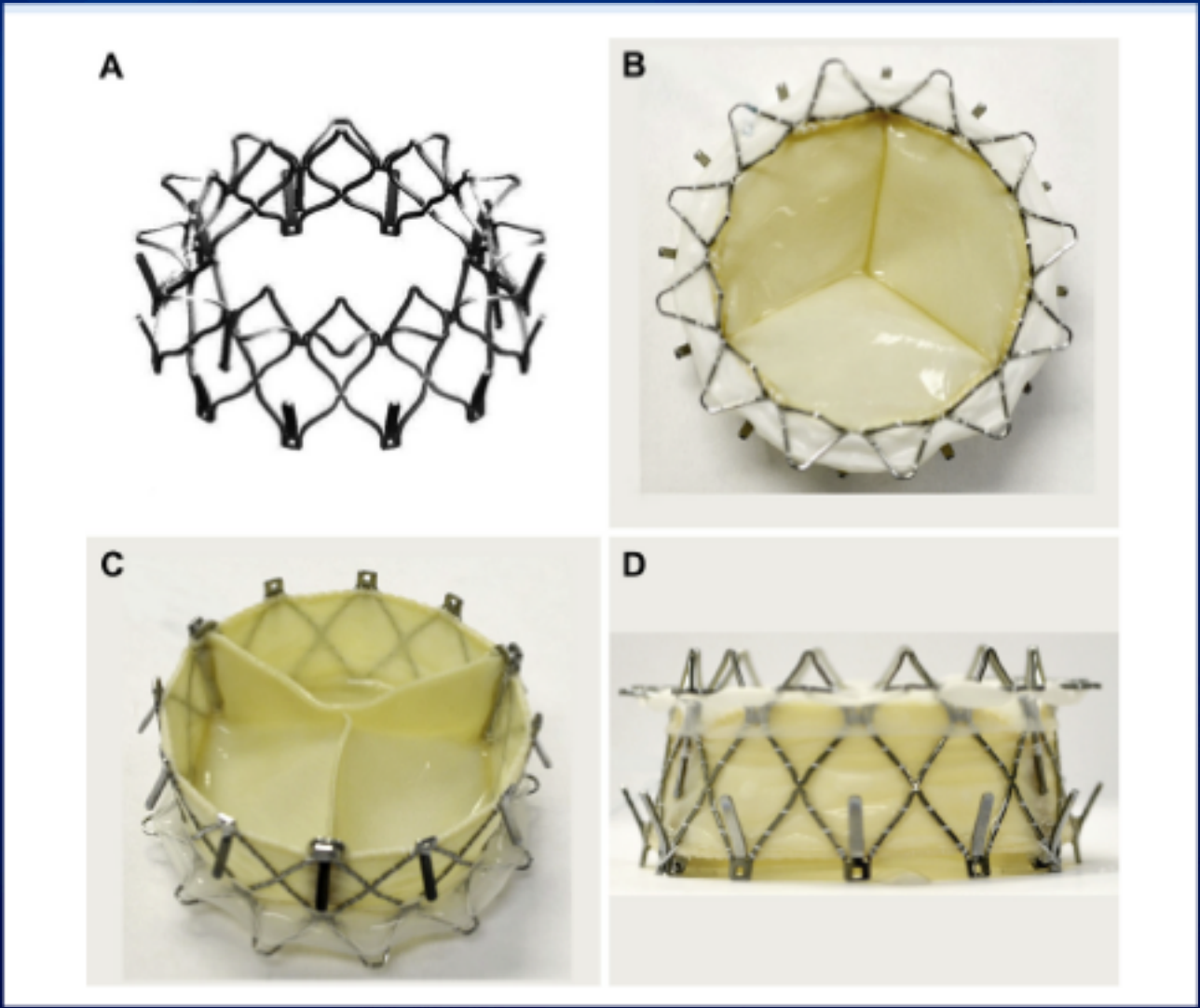
Navigate Valved Stent



- Nitinol alloy stent
- Equine pericardial leaflets
- Conical shape
- Self-expanding
- Anchoring by 12 active fixation components on ventricular and atrial annular surfaces
- Transatrial and Jugular approaches

Navia J et al. JACC BTS 2018
Kapadia S et al. Circ CV Interv 2017

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Conclusions

- Severe TR associated with poor prognosis
- Surgery for TR is high risk and performed infrequently
- Percutaneous therapies for TR are badly needed
- Several promising techniques are under investigation including:
  - Leaflet plication
  - Annuloplasty
  - Spacer therapy
  - Replacement

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Thank you!

Eleid.mackram@mayo.edu