Cedars Sinai
Smidt Heart Institute

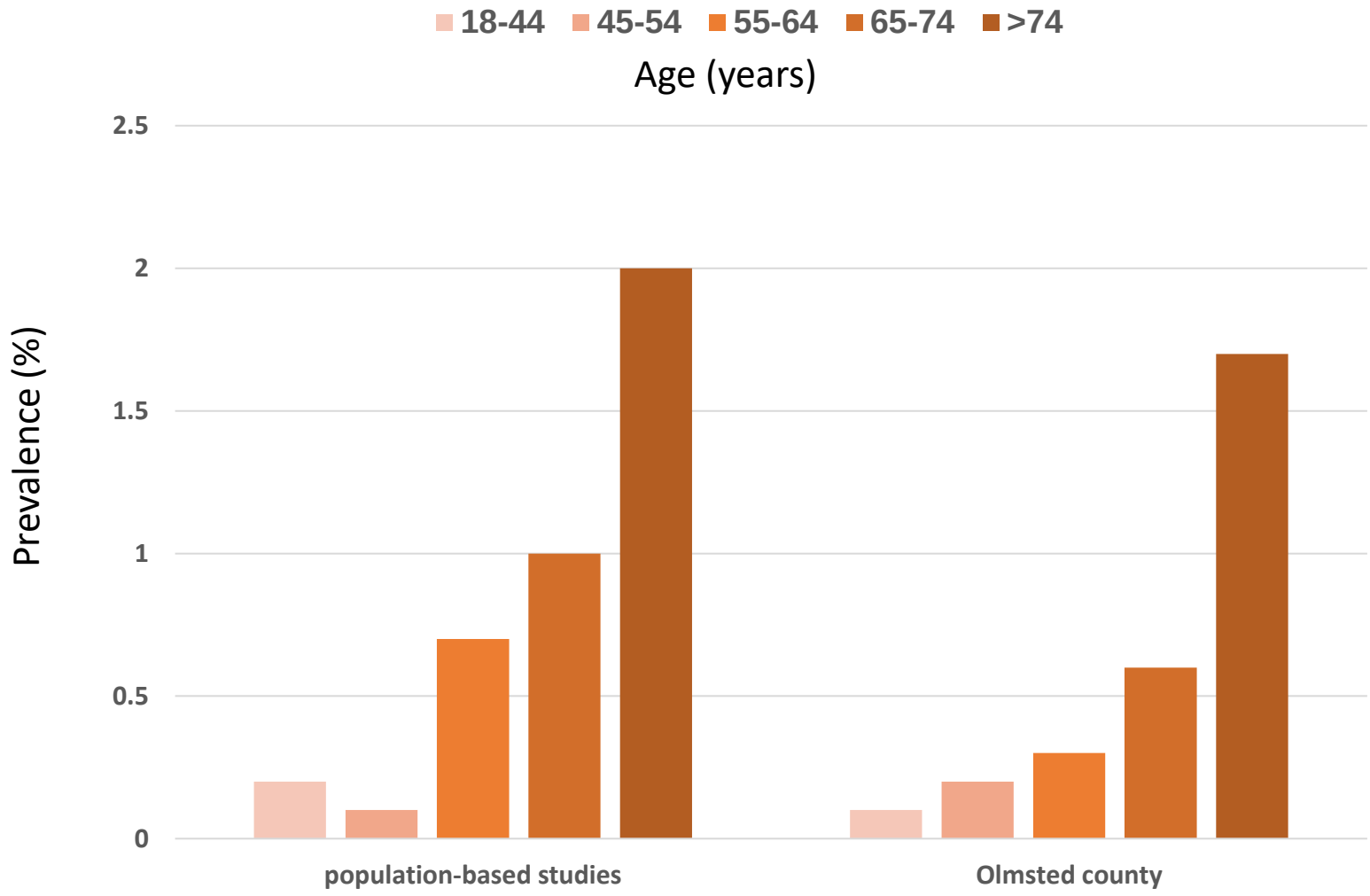
TAVR for Aortic Regurgitation

Raj R. Makkar, MD
Stephen Corday Chair in Interventional Cardiology
Vice President, Cardiac Interventions and Innovation
Smidt Heart Institute, Cedars Sinai Medical Center
Los Angeles

Prevalence of aortic regurgitation

Cedars Sinai
Smidt Heart Institute

A population-based study



Guidelines limited for TAVR

Cedars Sinai
Smidt Heart Institute

2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease

Recommendations for Timing of Intervention for Chronic AR
Referenced studies that support the recommendations are summarized in [illegible].

COR	LOE	Recommendations
1	B-NR	1. In symptomatic patients with severe AR (Stage D), aortic valve surgery is indicated regardless of LV systolic function.[1–7]
1	B-NR	2. In asymptomatic patients with chronic severe AR and LV systolic dysfunction (LVEF ≤55%) (Stage C2), aortic valve surgery is indicated if no other cause for systolic dysfunction is identified.[3,5,8–12]
1	C-EO	3. In patients with severe AR (Stage C or D) who are undergoing cardiac surgery for other indications, aortic valve surgery is indicated.
2a	B-NR	4. In asymptomatic patients with severe AR and normal LV systolic function (LVEF >55%), aortic valve surgery is reasonable when the LV is severely enlarged (LVESD >50 mm or indexed LVESD >25 mm/m²) (Stage C2).[10,11,13–24]
2a	C-EO	5. In patients with moderate AR (Stage B) who are undergoing cardiac or aortic surgery for other indications, aortic valve surgery is reasonable.
2b	B-NR	6. In asymptomatic patients with severe AR and normal LV systolic function at rest (LVEF >55%; Stage C1) and low surgical risk, aortic valve surgery may be considered when there is a progressive decline in LVEF on at least 3 serial studies to the low-normal range (LVEF 55% to 60%) or a progressive increase in LV dilation into the severe range (LV end-diastolic dimension [LVEDD] >65 mm).[12,16,17,20,25–28]
3: Harm	B-NR	7. In patients with isolated severe AR who have indications for SAVR and are candidates for surgery, TAVI should not be performed.[29–32]

3: Harm	B-NR	7. In patients with isolated severe AR who have indications for SAVR and are candidates for surgery, TAVI should not be performed.[29–32]

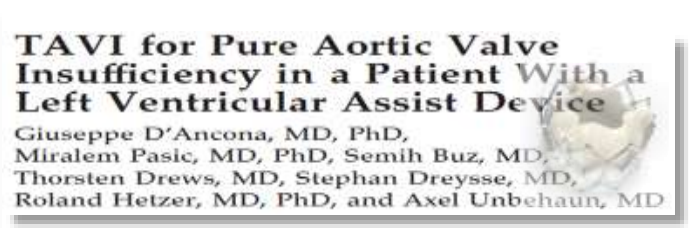
"TAVI is rarely feasible, and then only in carefully selected patients with severe AR and HF who have a prohibitive surgical risk and in whom valvular calcification and annular size are appropriate for a transcatheter approach."

TAVI for Pure Severe Native AR

Cedars Sinai
Smidt Heart Institute

Transcatheter Aortic Valve Implantation for Pure Severe Native Aortic Valve Regurgitation

David A. Roy, MD, FRACP, MRCPI,* Ulrich Schaefer, MD, PhD,† Victor Guetta, MD,‡ David Hildick-Smith, MD,§ Helge Möllmann, MD,‖ Nicholas Dumonteil, MD,¶ Thomas Modine, MD,# Johan Bosmans, MD,** Anna Sonia Petronio, MD,†† Neil Moat, MBBS, MS,‡‡ Axel Linke, MD,§§ Cesar Moris, MD,‖‖ Didier Champagnac, MD,¶¶ Radoslaw Parma, MD, PhD,## Andrzej Ochala, MD,## Diego Medvedofsky, MD,‡ Tiffany Patterson, MD,‡‡ Felix Woitek, MD,§§ Marjan Jahangiri, MD,* Jean-Claude Laborde, MD,* Stephen J. Brecker, MD*



TAVI for Pure Aortic Valve Insufficiency in a Patient With a Left Ventricular Assist Device

Giuseppe D'Ancona, MD, PhD, Miralem Pasic, MD, PhD, Semih Buz, MD, Thorsten Drews, MD, Stephan Dreysse, MD, Roland Hetzer, MD, PhD, and Axel Unbehaun, MD

Initial German Experience With Transapical Implantation of a Second-Generation Transcatheter Heart Valve for the Treatment of Aortic Regurgitation

Moritz Seiffert, MD,* Ralf Bader, MD,† Utz Kappert, MD,† Ardawan Rastan, MD,† Stephan Krapf, MD,† Sabine Bleiziffer, MD,¶ Steffen Hofmann, MD,# Martin Arnold, MD,** Klaus Kallenbach, MD,†† Lenard Conradi, MD,* Friederike Schlingloff, MD,† Manuel Wilbring, MD,† Ulrich Schäfer, MD,† Patrick Diemert, MD,* Hendrik Treede, MD*

A New Transcatheter Aortic Valve Replacement System for Predominant Aortic Regurgitation Implantation of the J-Valve and Early Outcome

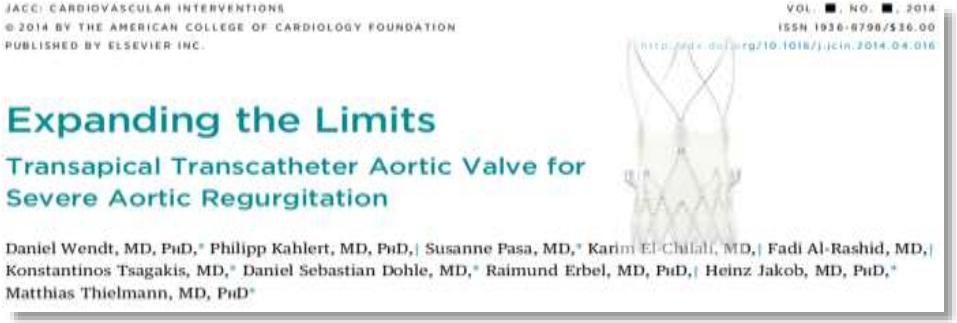
Lai Wei, MD,* Huan Liu, MD,* Liming Zhu, MD,* Ye Yang, MD,* Jiayu Zheng, MD,* Kefang Guo, MD,† Hong Luo, MD,† Weipeng Zhao, MD,† Xue Yang, MD,† Aikebaier Maimaiti, MD,* Chundeng Wang, MD*

The Helio transcatheter aortic dock for patients with aortic regurgitation

Marco Barbanti[1], MD; Jian Ye[1], MD; Sanjeevan Pasupati[1], MD; Adam El-Gamel[2], MD, FRCS; John G. Webb[1]*, MD

CoreValve implantation for severe aortic regurgitation: a multicentre registry

Luca Testa[1]*, MD, PhD; Azeem Latib[2], MD; Marco Luciano Rossi[2], MD; Federico De Marco[2], MD; Marco De Carlo[2], MD; Claudia Fiorina[2], MD; Jacopo Oreglia[2], MD; Anna Sonia Petronio[2], MD; Federica Ettori[2], MD; Stefano De Servi[2], MD; Silvio Klugmann[2], MD; Gian Paolo Ussia[2], MD; Corrado Tamburino[2], MD; Paolo Panisi[2], MD; Nedy Brambilla[2], MD; Antonio Colombo[2], MD; Patrizia Presbitero[2], MD; Francesco Bedogni[2], MD



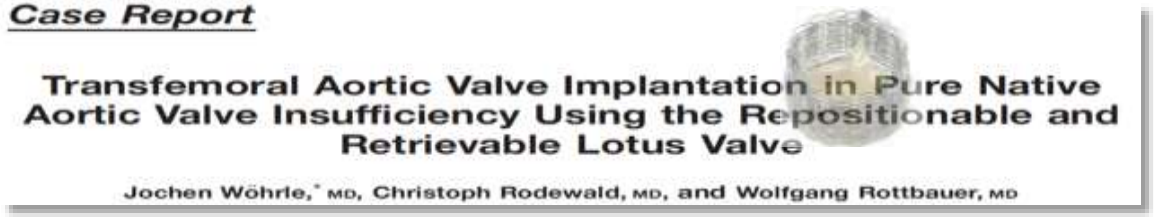
JACC: CARDIOVASCULAR INTERVENTIONS
© 2014 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER INC.

VOL. ■, NO. ■, 2014
ISSN 1936-8798/$36.00

Expanding the Limits

Transapical Transcatheter Aortic Valve for Severe Aortic Regurgitation

Daniel Wendt, MD, PhD,* Philipp Kahlert, MD, PhD,† Susanne Pasa, MD,* Karim El-Chilali, MD,† Fadi Al-Rashid, MD,† Konstantinos Tsagakis, MD,* Daniel Sebastian Dohle, MD,* Raimund Erbel, MD, PhD,† Heinz Jakob, MD, PhD,* Matthias Thielmann, MD, PhD*



Case Report

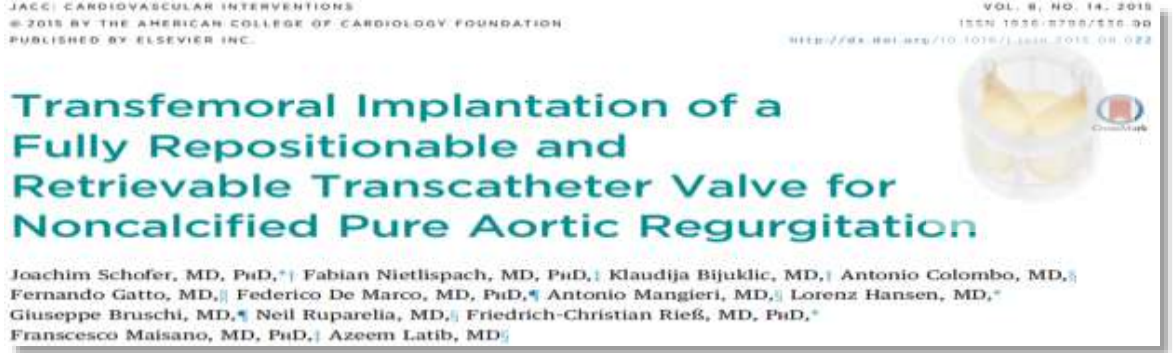
Transfemoral Aortic Valve Implantation in Pure Native Aortic Valve Insufficiency Using the Repositionable and Retrievable Lotus Valve

Jochen Wöhrle,* MD, Christoph Rodewald, MD, and Wolfgang Rottbauer, MD

Case Reports

Transcatheter aortic valve replacement for isolated aortic valve insufficiency: Experience with the Engager valve

Philipp Kiefer, MD, Joerg Seeburger, MD, PhD, Friedrich W. Mohr, MD, PhD, and David M. Holzhey, MD, PhD, Leipzig, Germany



JACC: CARDIOVASCULAR INTERVENTIONS
© 2015 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER INC.

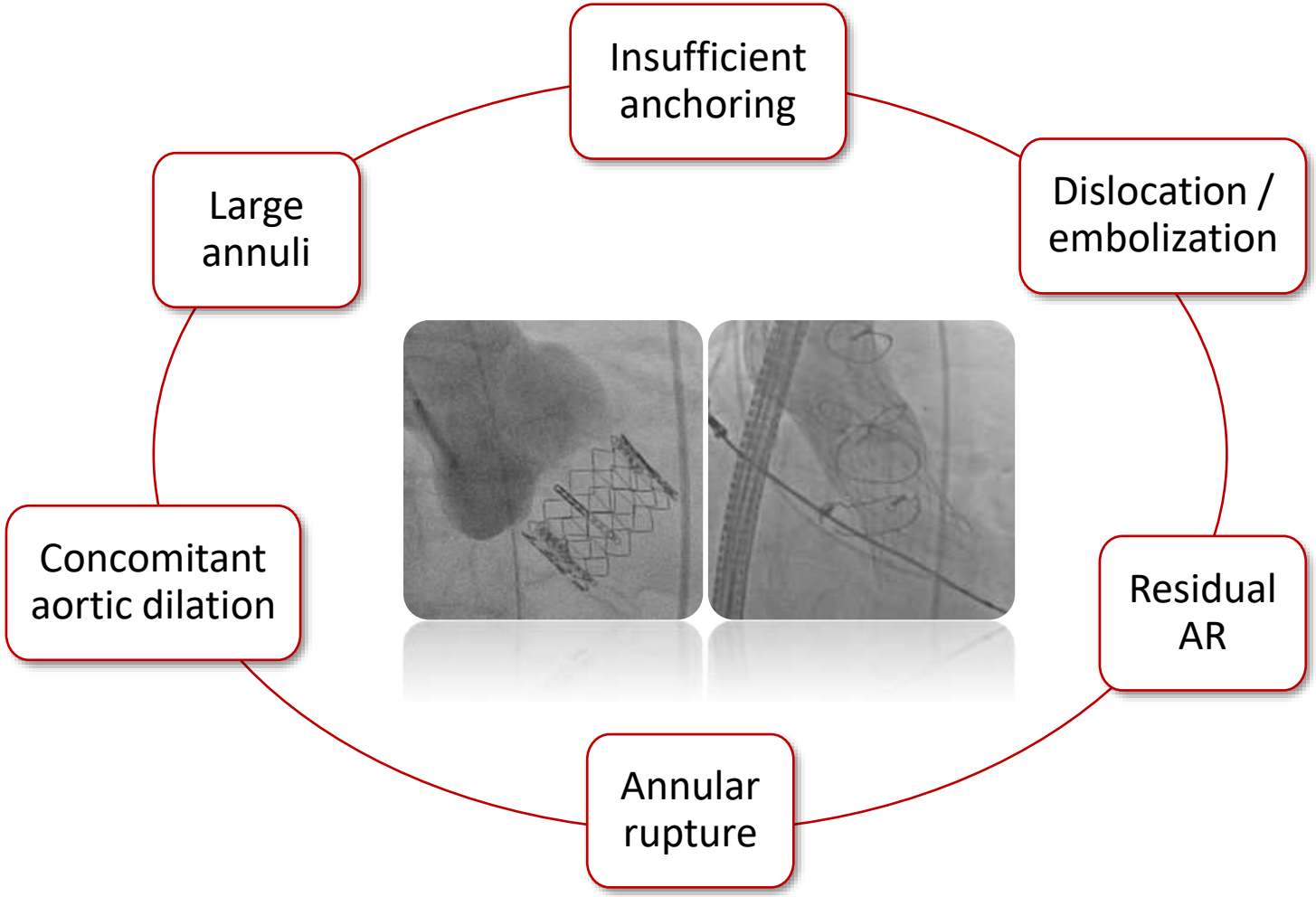
VOL. 8, NO. 14, 2015
ISSN 1936-8798/$36.00

Transfemoral Implantation of a Fully Repositionable and Retrievable Transcatheter Valve for Noncalcified Pure Aortic Regurgitation

Joachim Schofer, MD, PhD,*† Fabian Nietlispach, MD, PhD,‡ Klaudija Bijuklic, MD,† Antonio Colombo, MD,§ Fernando Gatto, MD,‖ Federico De Marco, MD, PhD,¶ Antonio Mangieri, MD,§ Lorenz Hansen, MD,* Giuseppe Bruschi, MD,¶ Neil Ruparelia, MD,‖ Friedrich-Christian Rieß, MD, PhD,* Franscesco Maisano, MD, PhD,† Azeem Latib, MD§

Challenges in Treatment of Pure AR

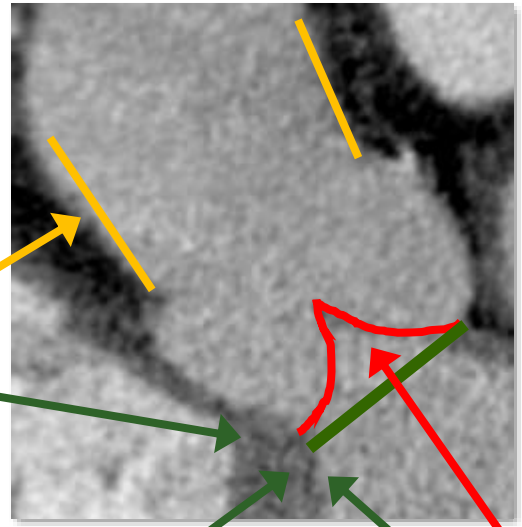
Cedars Sinai
Smidt Heart Institute



Anchoring Mechanisms

Cedars Sinai
Smidt Heart Institute

Annulus + Aorta



Annulus only

Leaflets + Annulus

Transcatheter Aortic Valve Replacement in Pure Native Aortic Valve Regurgitation

Sung-Han Yoon, MD,[a] Tobias Schmidt, MD,[b] Sabine Bleiziffer, MD,[c] Niklas Schofer, MD,[d] Claudia Fiorina, MD,[e] Antonio J. Munoz-Garcia, MD,[f] Ermela Yzeiraj, MD,[g] Ignacio J. Amat-Santos, MD,[h] Didier Tchetche, MD,[i] Christian Jung, MD,[j] Buntaro Fujita, MD,[k] Antonio Mangieri, MD,[l] Marcus-Andre Deutsch, MD,[c,m] Timm Ubben, MD,[b] Florian Deuschl, MD,[d] Shingo Kuwata, MD,[n] Chiara De Biase, MD,[i] Timothy Williams, MD,[o] Abhijeet Dhoble, MD,[p] Won-Keun Kim, MD,[q] Enrico Ferrari, MD,[r] Marco Barbanti, MD,[s] E. Mara Vollema, MD,[t] Antonio Miceli, MD,[u] Cristina Giannini, MD,[v] Guiherme F. Attizzani, MD,[w] William K.F. Kong, MD,[x] Enrique Gutierrez-Ibanes, MD,[y] Victor Alfonso Jimenez Diaz, MD,[z] Harindra C. Wijeysundera, MD,[aa] Hidehiro Kaneko, MD,[bb] Tarun Chakravarty, MD,[a] Moody Makar, MD,[a] Horst Sievert, MD,[cc] Christian Hengstenberg, MD,[m,dd] Bernard D. Prendergast, MD,[ee] Flavien Vincent, MD,[ff] Mohamed Abdel-Wahab, MD,[gg] Luis Nombela-Franco, MD,[hh] Miriam Silaschi, MD,[ii] Giuseppe Tarantini, MD,[jj] Christian Butter, MD,[bb] Stephan M. Ensminger, MD,[k] David Hildick-Smith, MD,[o] Anna Sonia Petronio, MD,[v] Wei-Hsian Yin, MD,[kk] Federico De Marco, MD,[ll] Luca Testa, MD,[ll] Nicolas M. Van Mieghem, MD,[mm] Brian K. Whisenant, MD,[nn] Karl-Heinz Kuck, MD,[b] Antonio Colombo, MD,[l] Saibal Kar, MD,[a] Cesar Moris, MD,[oo] Victoria Delgado, MD,[t] Francesco Maisano, MD,[n] Fabian Nietlispach, MD,[n] Michael J. Mack, MD,[pp] Joachim Schofer, MD,[g] Ulrich Schaefer, MD,[d] Jeroen J. Bax, MD,[t] Christian Frerker, MD,[b] Azeem Latib, MD,[l] Raj R. Makkar, MD[a]

A total of **331 patients** undergoing TAVR for pure native aortic insufficiency at 40 centers from Europe, North America and Asia-Pacific were included from the International multicenter registry

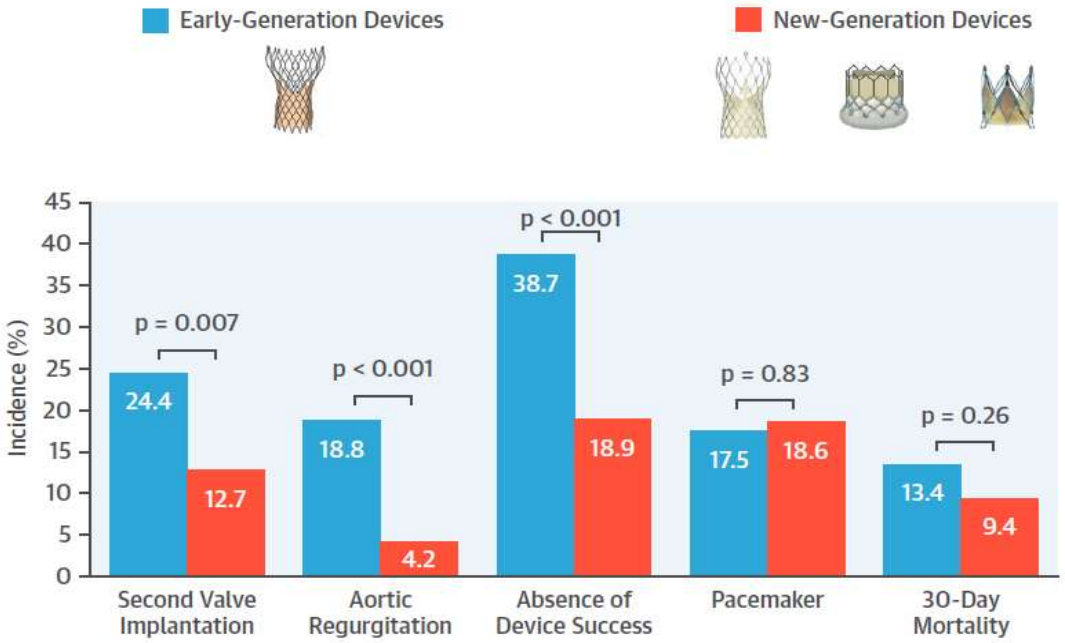
Yoon, S.-H. et al. J Am Coll Cardiol. 2017;70(22):2752–63.

Transcatheter Aortic Valve Replacement in Pure Native Aortic Valve Regurgitation

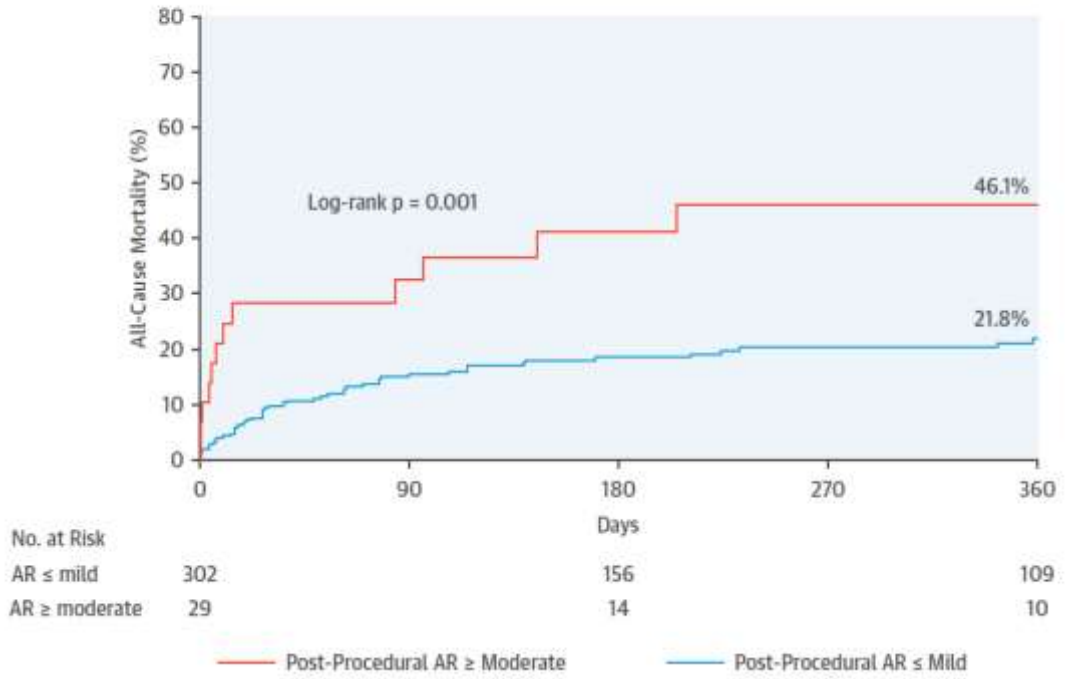
Cedars Sinai
Smidt Heart Institute

A total of **331 patients** undergoing TAVR for pure native aortic insufficiency at 40 centers from Europe, North America and Asia-Pacific were included from the International multicenter registry

Outcomes According to Devices



Mortality and Post-Procedural Aortic Regurgitation



Yoon, S.-H. et al. J Am Coll Cardiol. 2017;70(22):2752-63.

Aortic Regurgitation: Self-Expanding valve (x1)

74-year-old male

CLINICAL PRESENTATION

- Shortness of breath on exertion

CO-MORBIDITIES

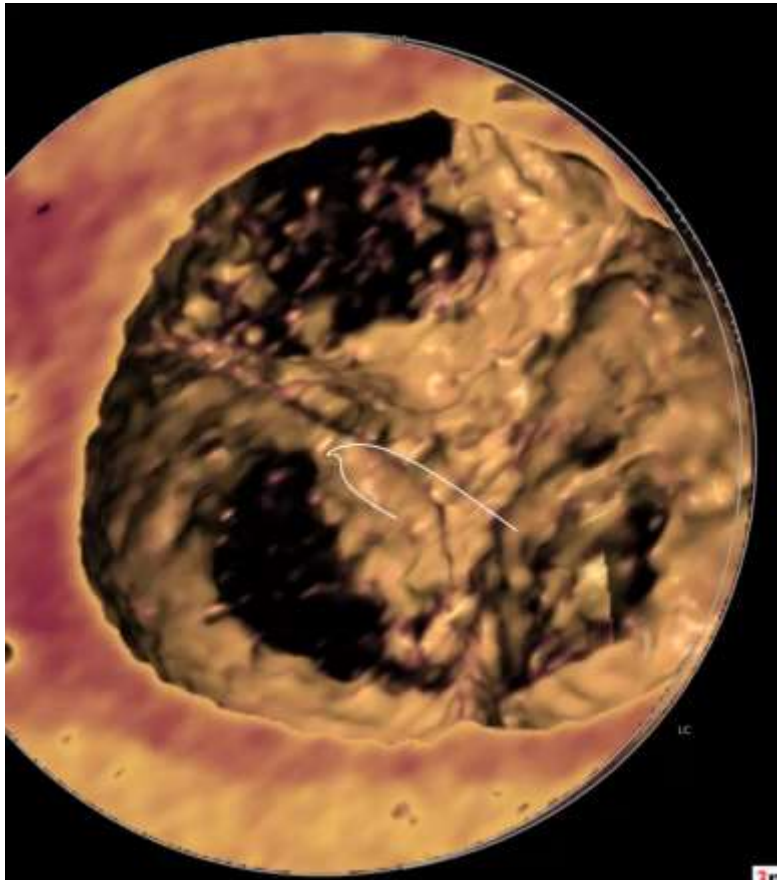
- Surgical mitral valve replacement (2017)
- Surgical tricuspid valve repair (2017)
- Pacemaker insertion

RISK SCORES

- STS: 7.8 %

TTE

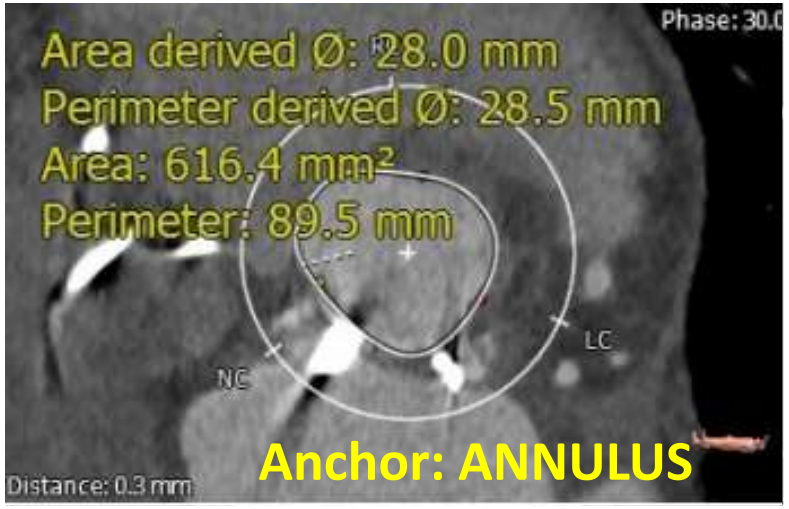
- EF: 50%
- Severe Aortic Regurgitation

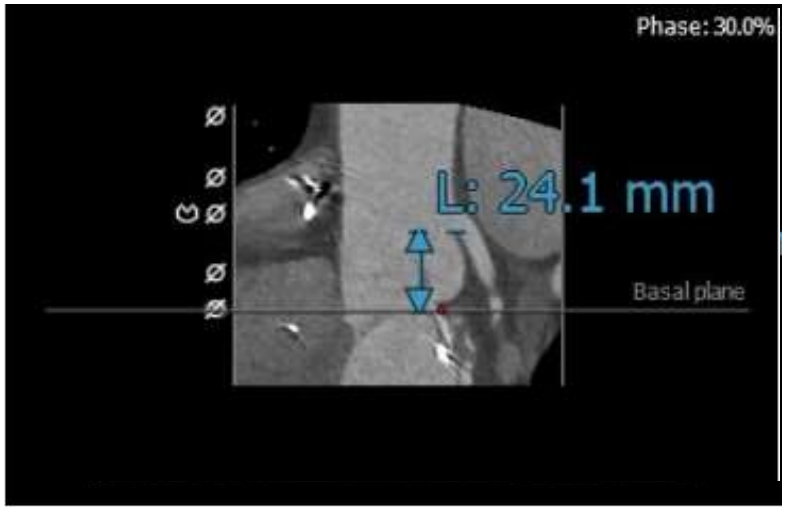


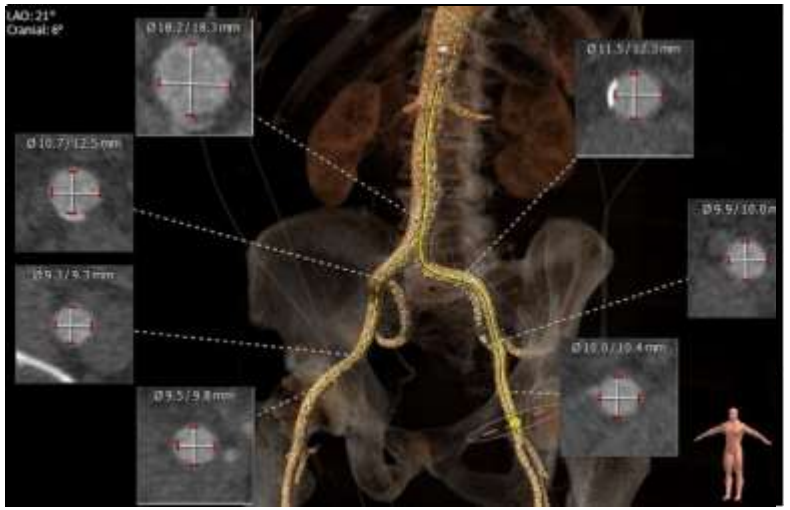
Aortic Regurgitation: Self-Expanding valve (x1)

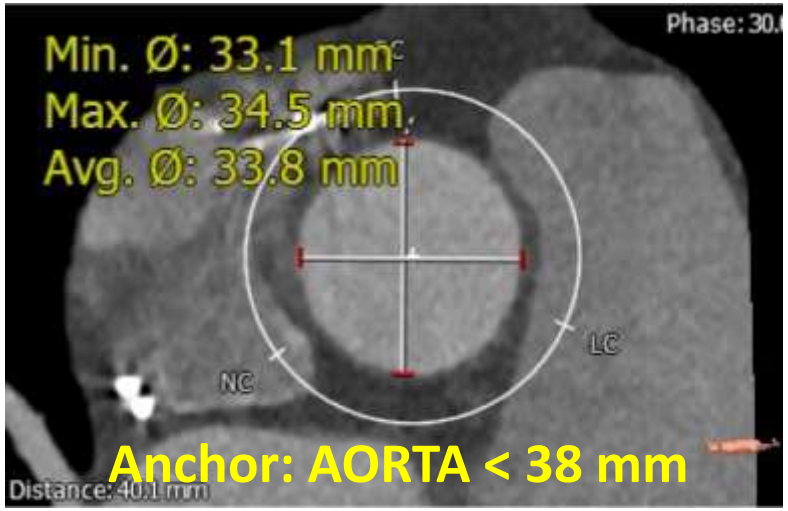
Cedars Sinai
Smidt Heart Institute

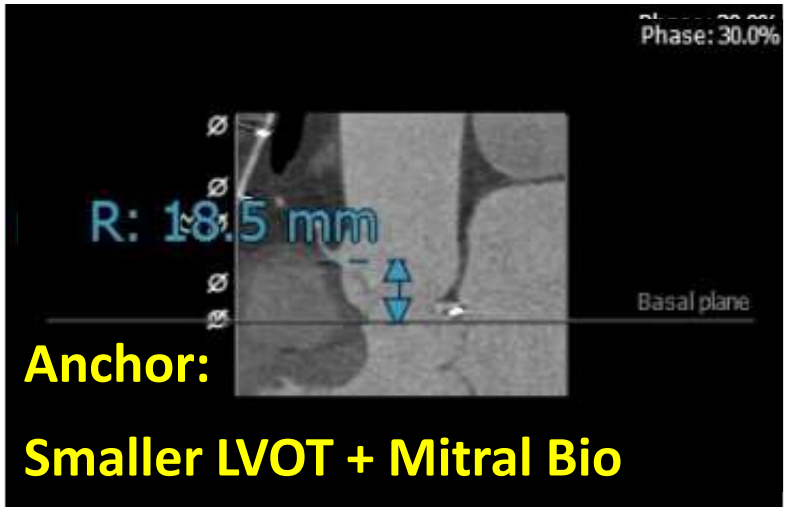
74-year-old male

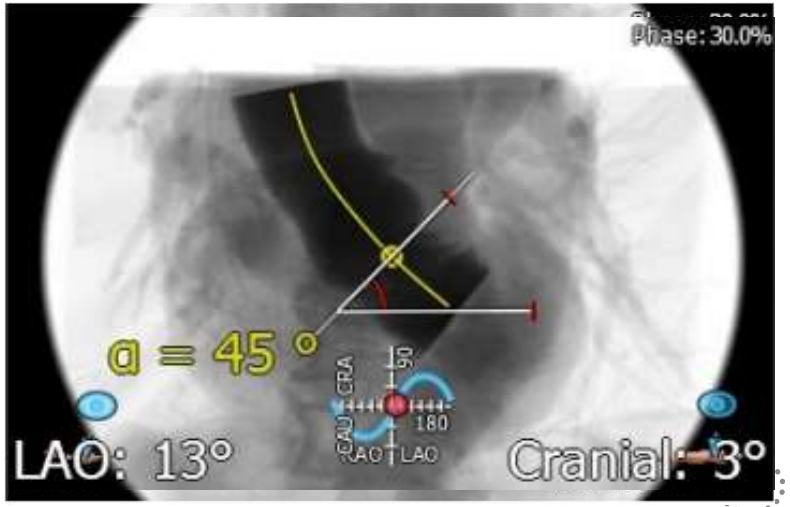












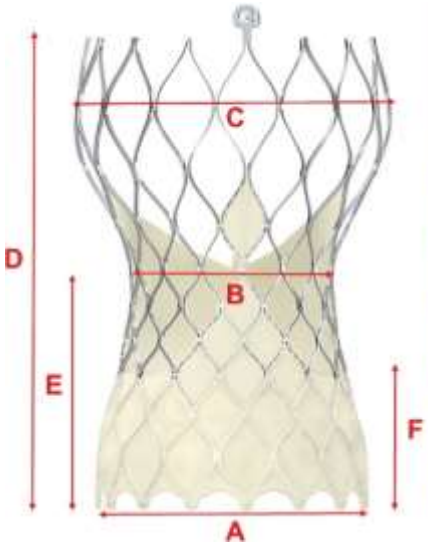
Aortic Regurgitation: Self-Expanding valve (x1)

Cedars Sinai
Smidt Heart Institute

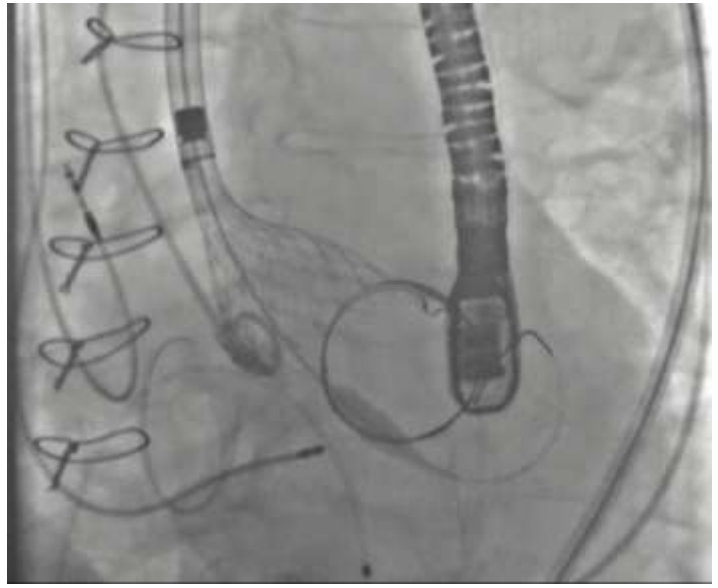
74-year-old male

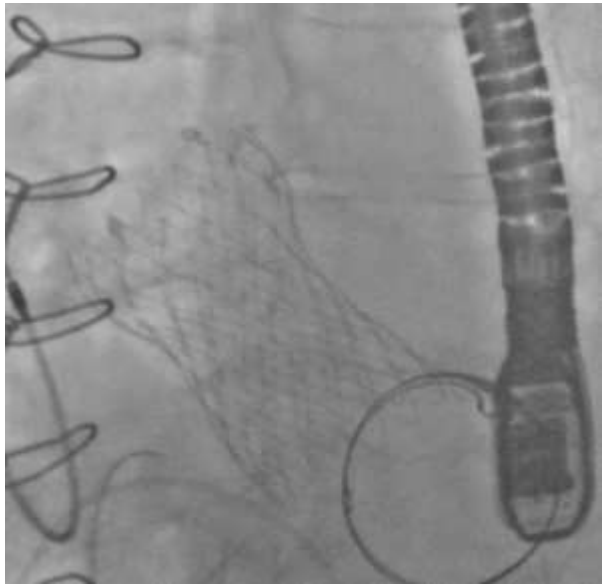
AORTA DIAMETER 33.8

ANNULUS 616mm^2



	34mm Evolut R
A. Inflow Diameter	34 mm
B. Waist Diameter	24 mm
C. Outflow Diameter	38 mm
D. Frame height	46 mm
E. Commissure Height	26 mm
F. Skirt Height	14 mm





MANAGEMENT

- **Treated with TAVR (34mm EVOLUT R)**
- **Discharged home on Day 1**

FOLLOW-UP

- **TTE: No PVL on discharge**
- **Awaiting 30-day follow-up**

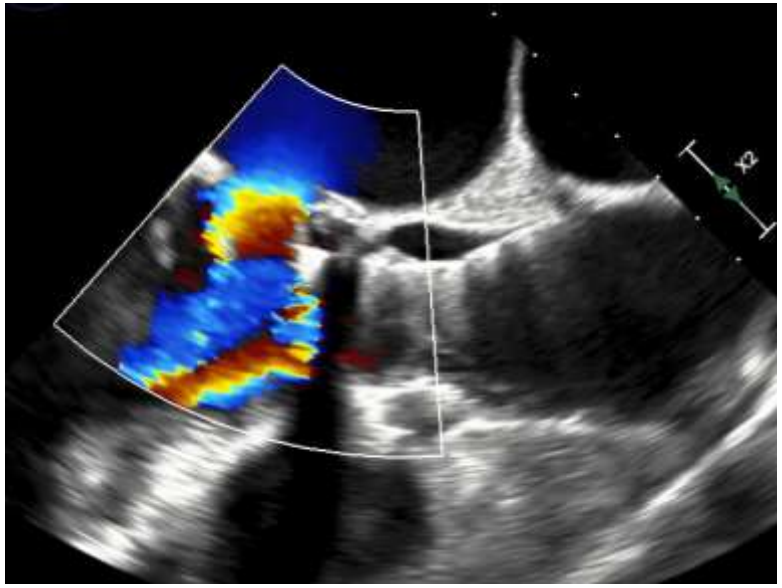
Aortic Regurgitation: Self-Expanding valve (x1)

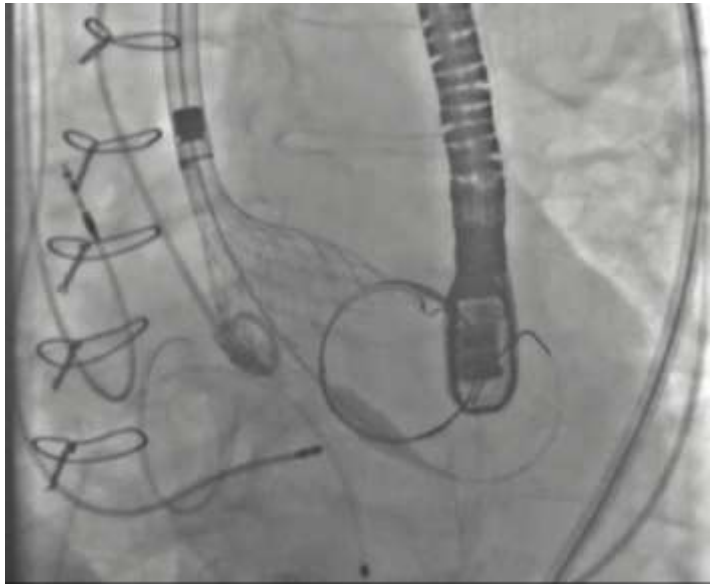
Cedars Sinai
Smidt Heart Institute

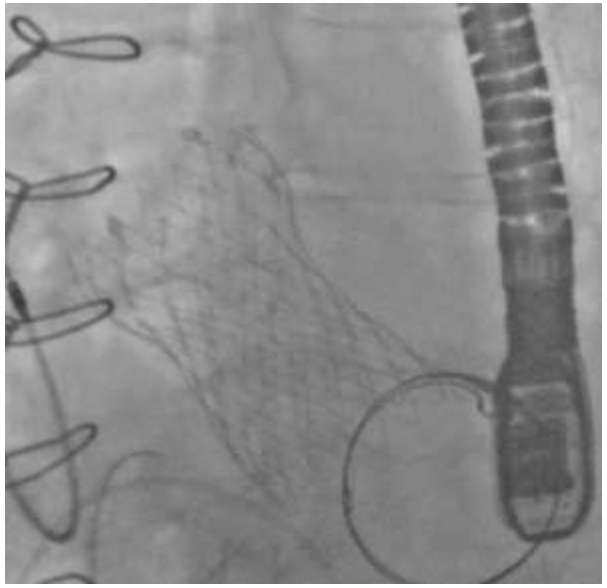
74-year-old male

AORTA DIAMETER 33.8

ANNULUS 616mm^2







MANAGEMENT

- **Treated with TAVR (34mm EVOLUT R)**
- **Discharged home on Day 1**

FOLLOW-UP

- **TTE: No PVL on discharge**

Aortic Regurgitation LVAD Case

74-year-old male

CLINICAL PRESENTATION

- Cardiogenic shock requiring inotrope support

CO-MORBIDITIES

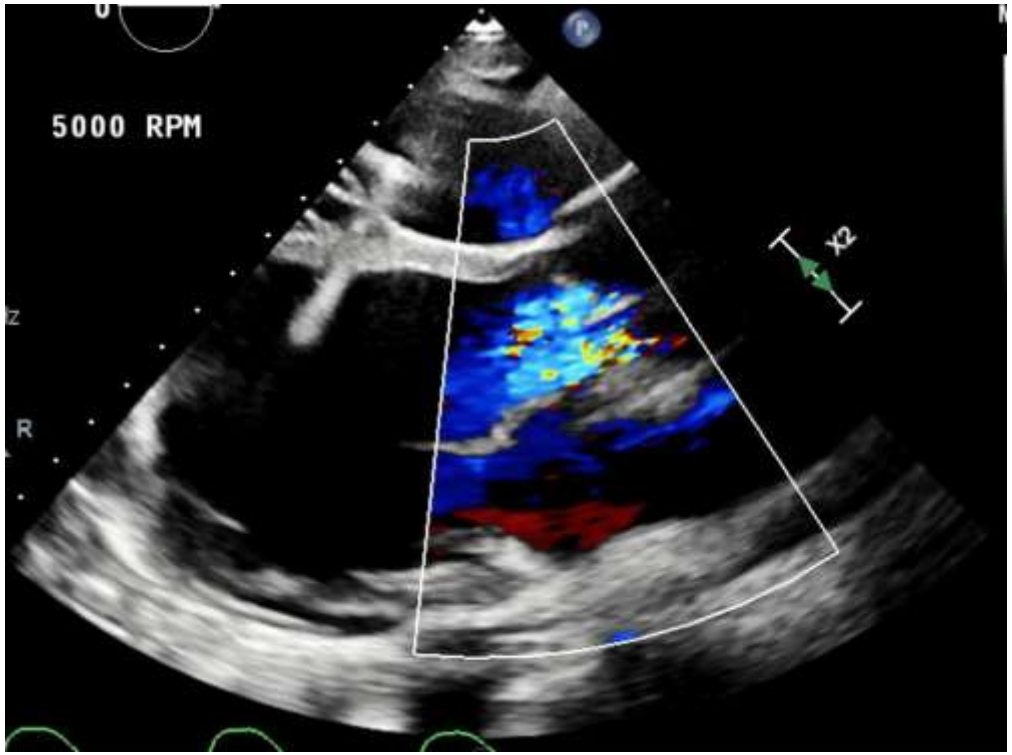
- DCM (EF 20%)
- HeartMate 3 LVAD
- ICD implanted

RISK SCORES

- STS: 9.1 %

TTE

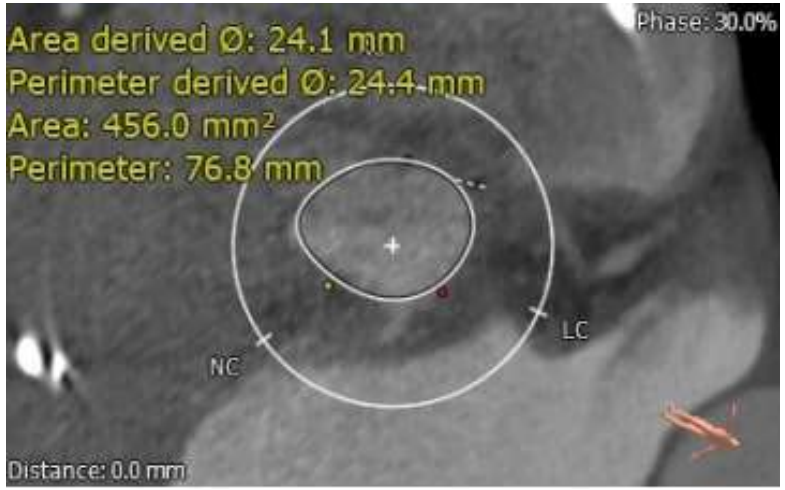
- EF: 20%
- Severe Aortic Regurgitation

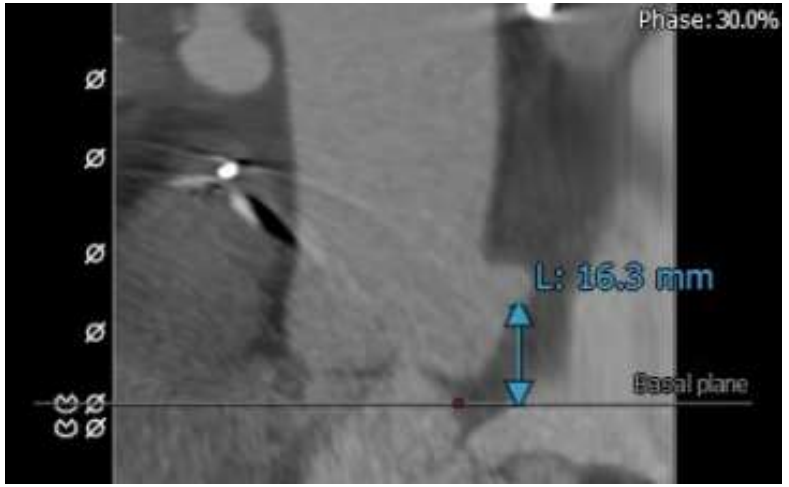


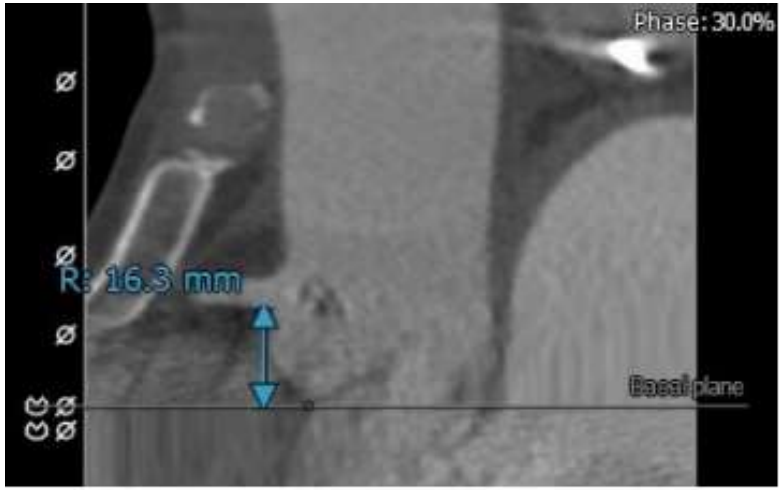
LVAD Case:
Self-expanding, backup BE

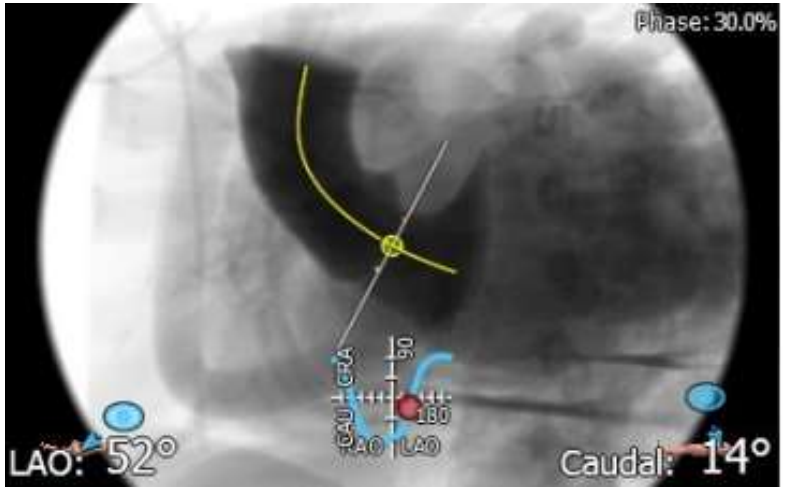
Cedars Sinai
Smidt Heart Institute

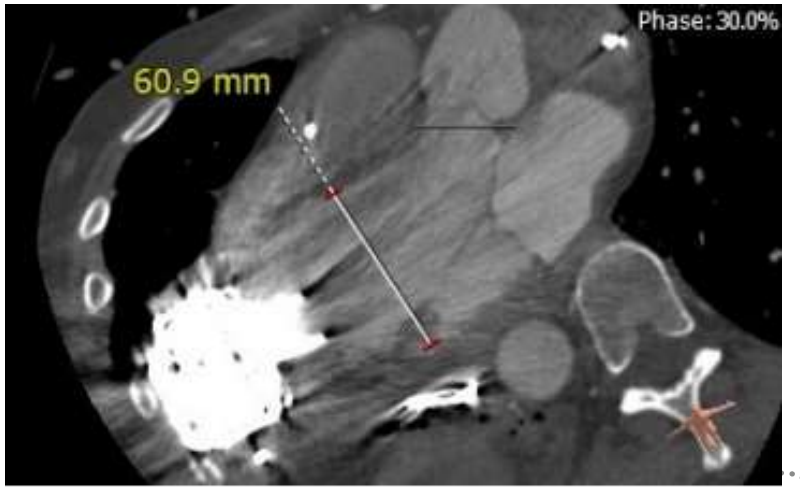
74-year-old male







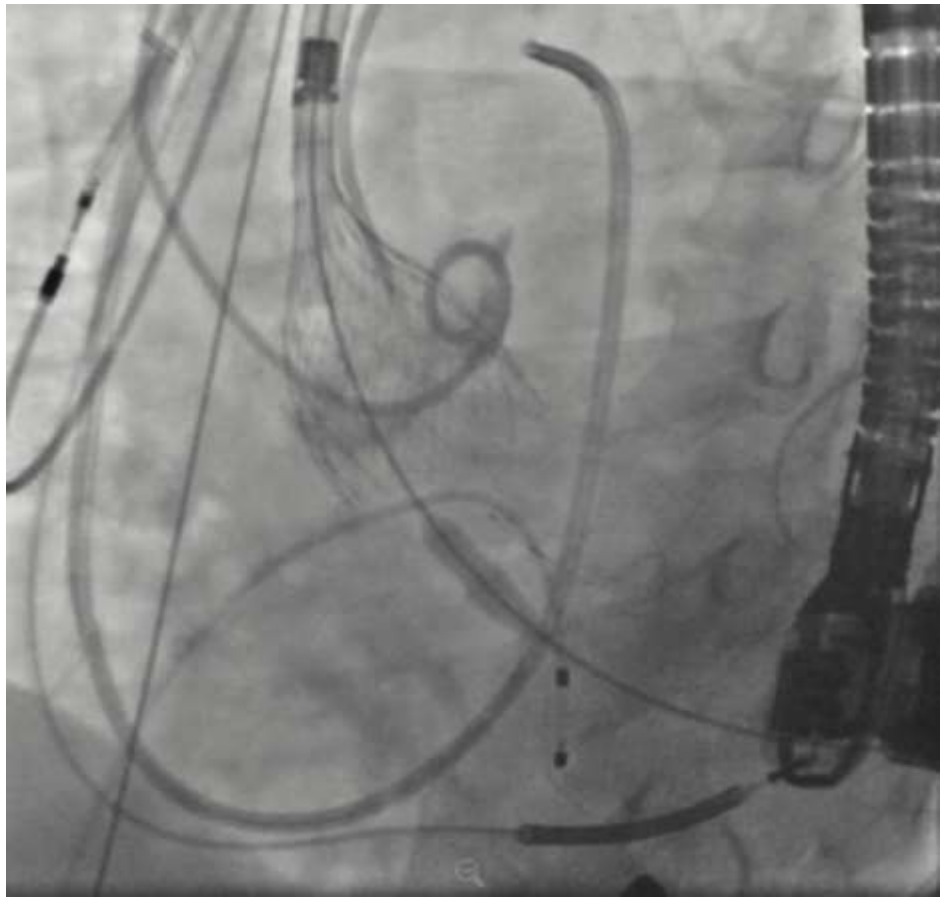




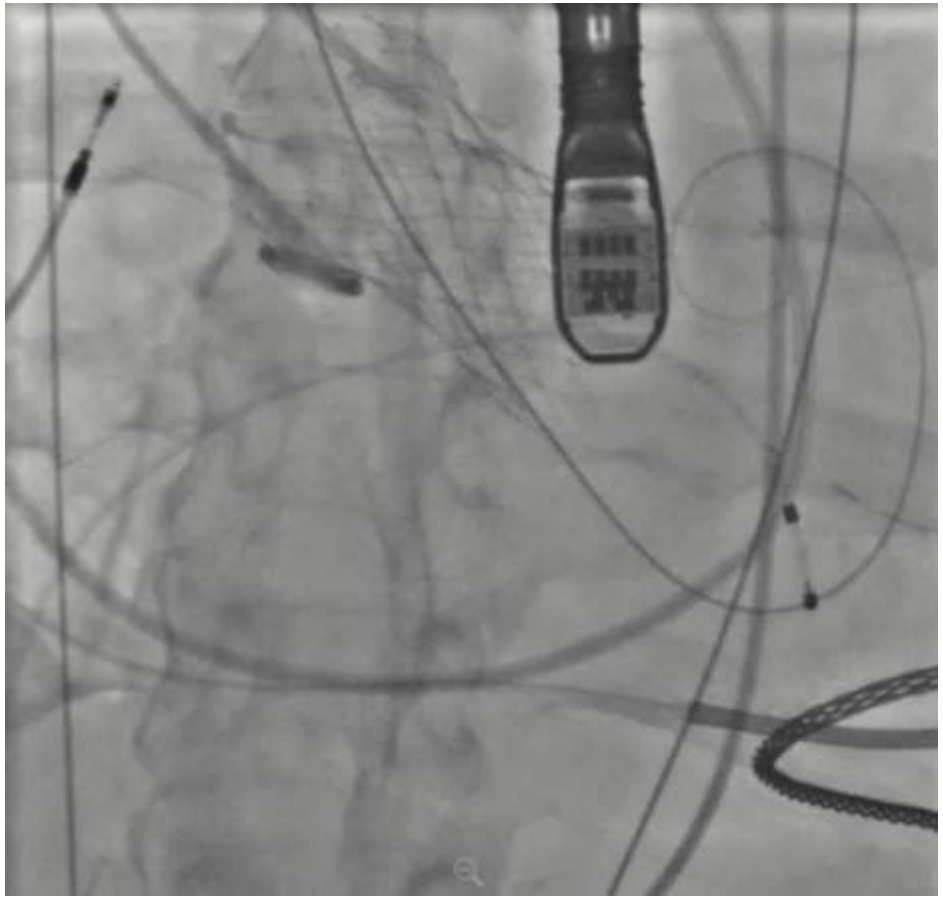
LVAD Case:
Self-expanding, backup BE

Cedars Sinai
Smidt Heart Institute

74-year-old male



29 mm Evolut Pro

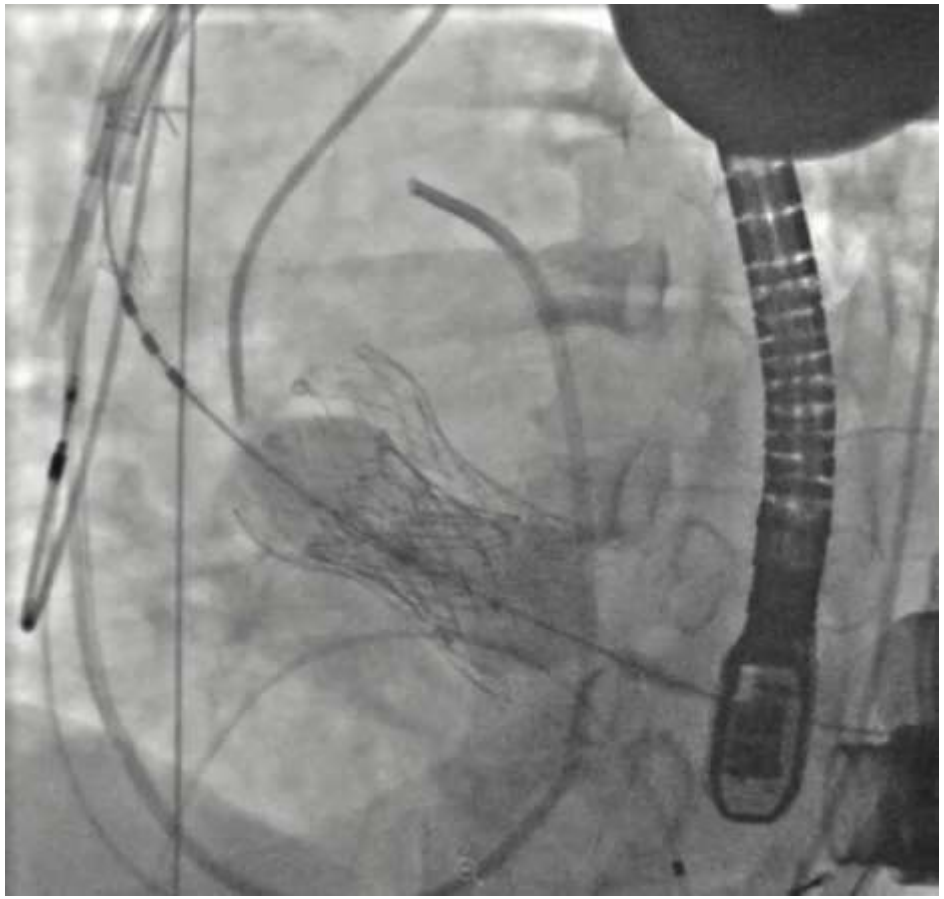


Valve pulled into LVOT by LVAD

LVAD Case:
Self-expanding, backup BE

Cedars Sinai
Smidt Heart Institute

74-year-old male

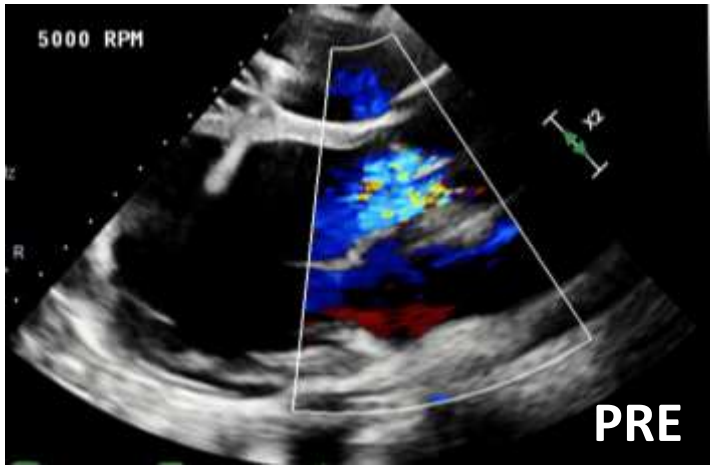


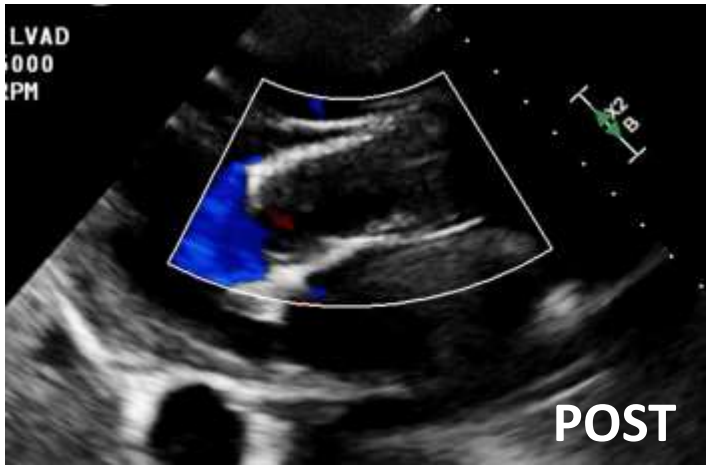
Transcatheter Aortic Valve Implantation:

- 26mm Sapien 3 deployed within previous prosthesis
- 3cc additional to nominal volume

Outcome:

- Off inotrope support and discharged home
- Mild PVL on discharge





57-year-old male s/p David procedure 4 years ago
Severe Aortic Regurgitation

Cedars Sinai
Smidt Heart Institute

Past medical history

- Type A aortic dissection and severe AI s/p David procedure and 28 Valsalva graft
- Type B aortic dissection s/p TEVAR using a Gore thoracic branch device
- Right carotid to left carotid artery bypass
- Left carotid artery to left subclavian artery bypass
- Chronic Kidney Disease
- NYHA Class III symptoms

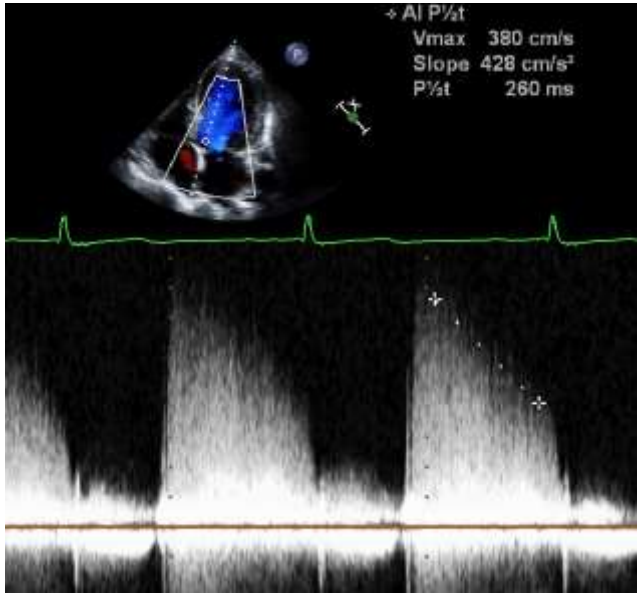
CT surgeon determined SAVR to be extremely difficult and risky

57-year-old male s/p David procedure 4 years ago

Severe Aortic Regurgitation

Cedars Sinai
Smidt Heart Institute

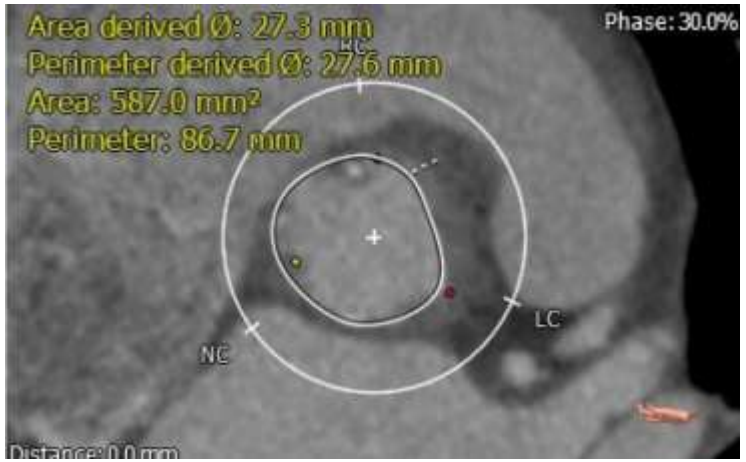
Severe AI



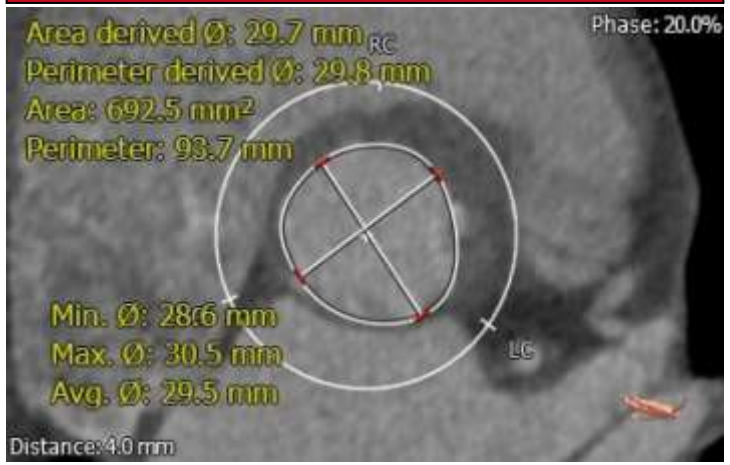
CT Analysis

Cedars Sinai
Smidt Heart Institute

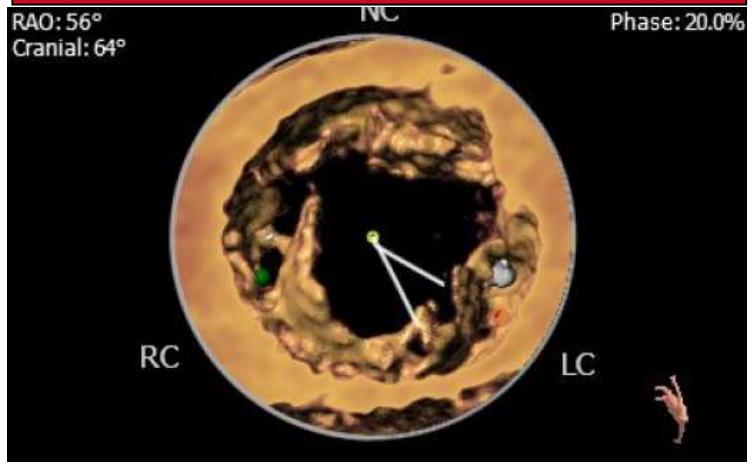
Annulus



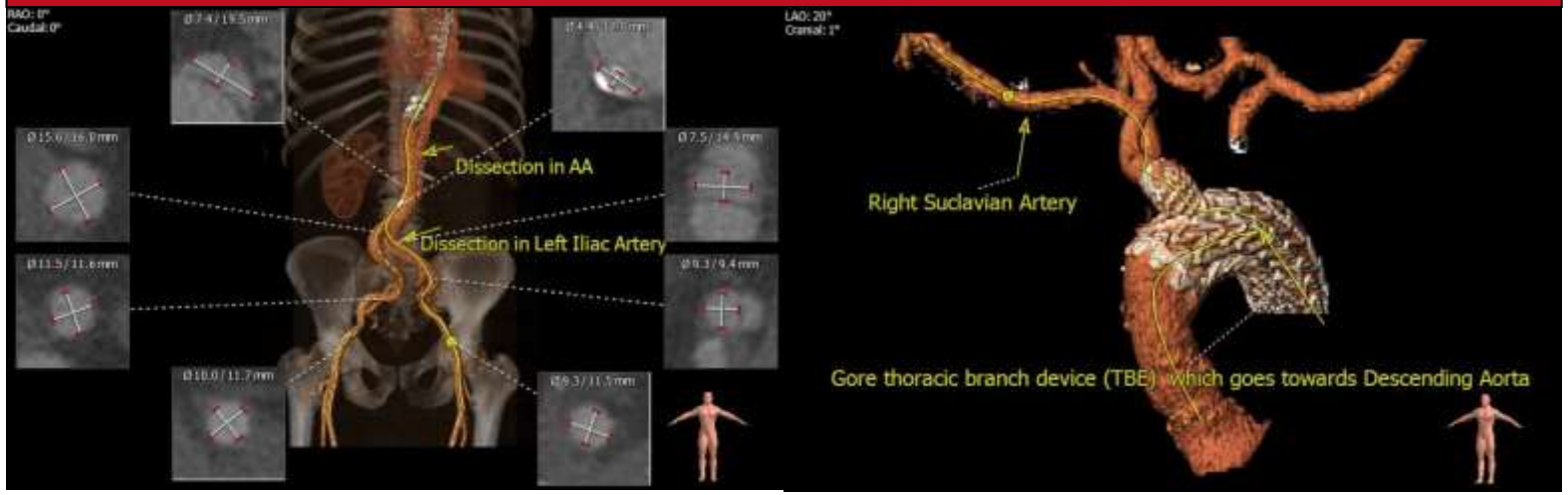
LVOT



No AV Calcium



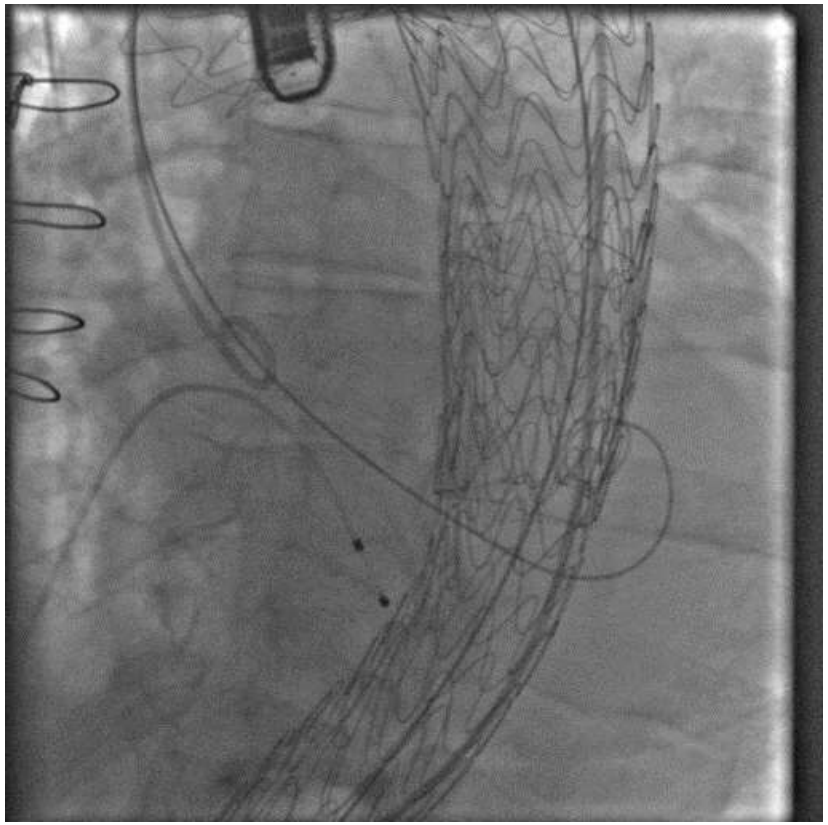
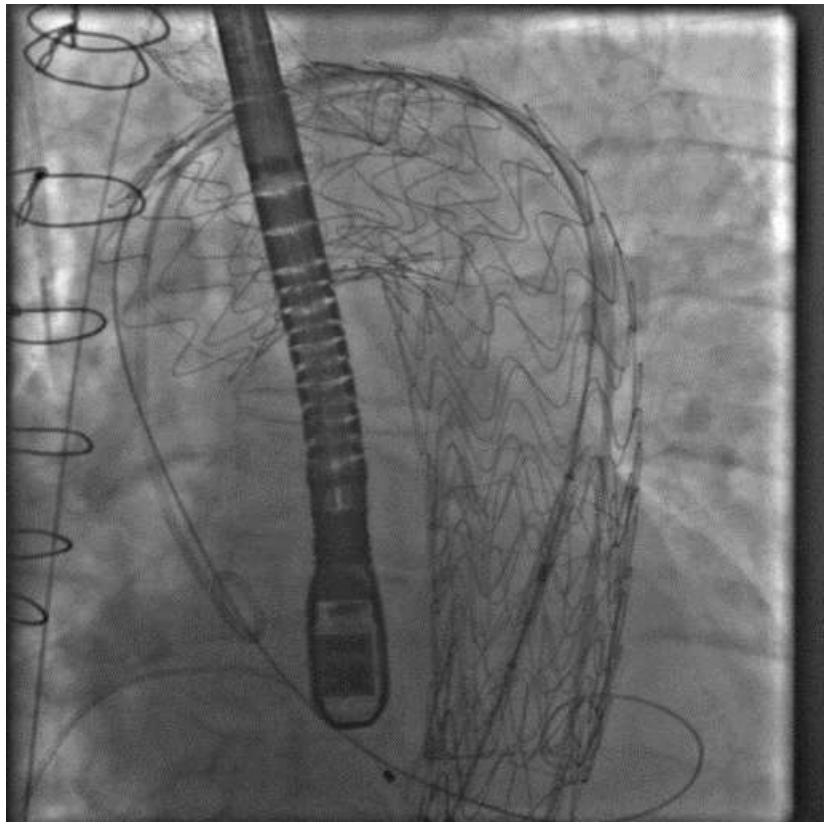
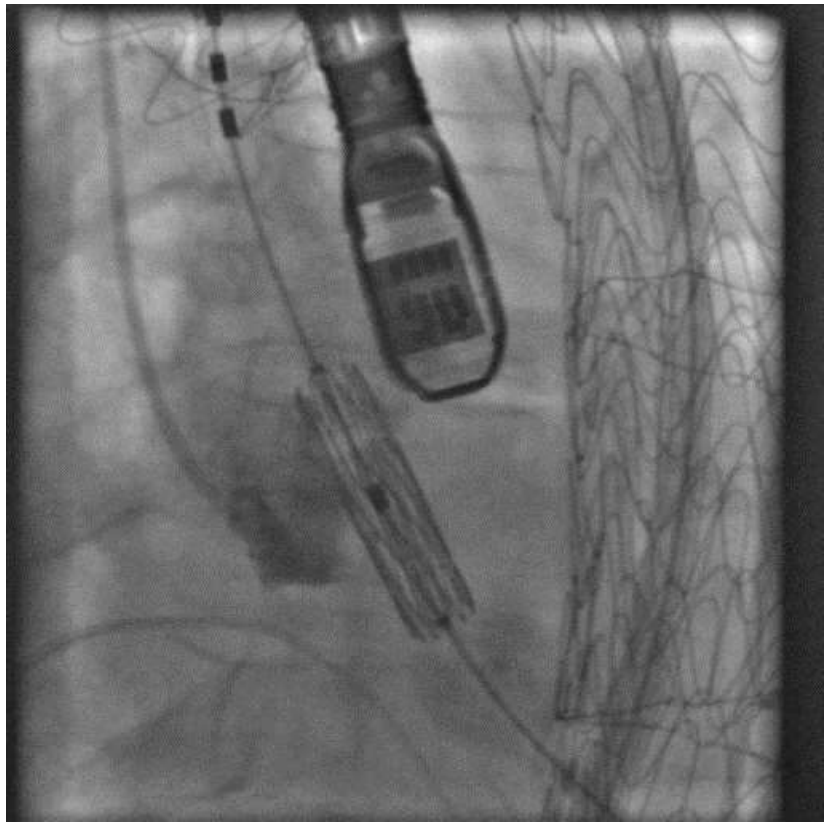
Difficult Access



TAVR with 29mm Sapien 3 via Transfemoral Approach

Cedars Sinai
Smidt Heart Institute

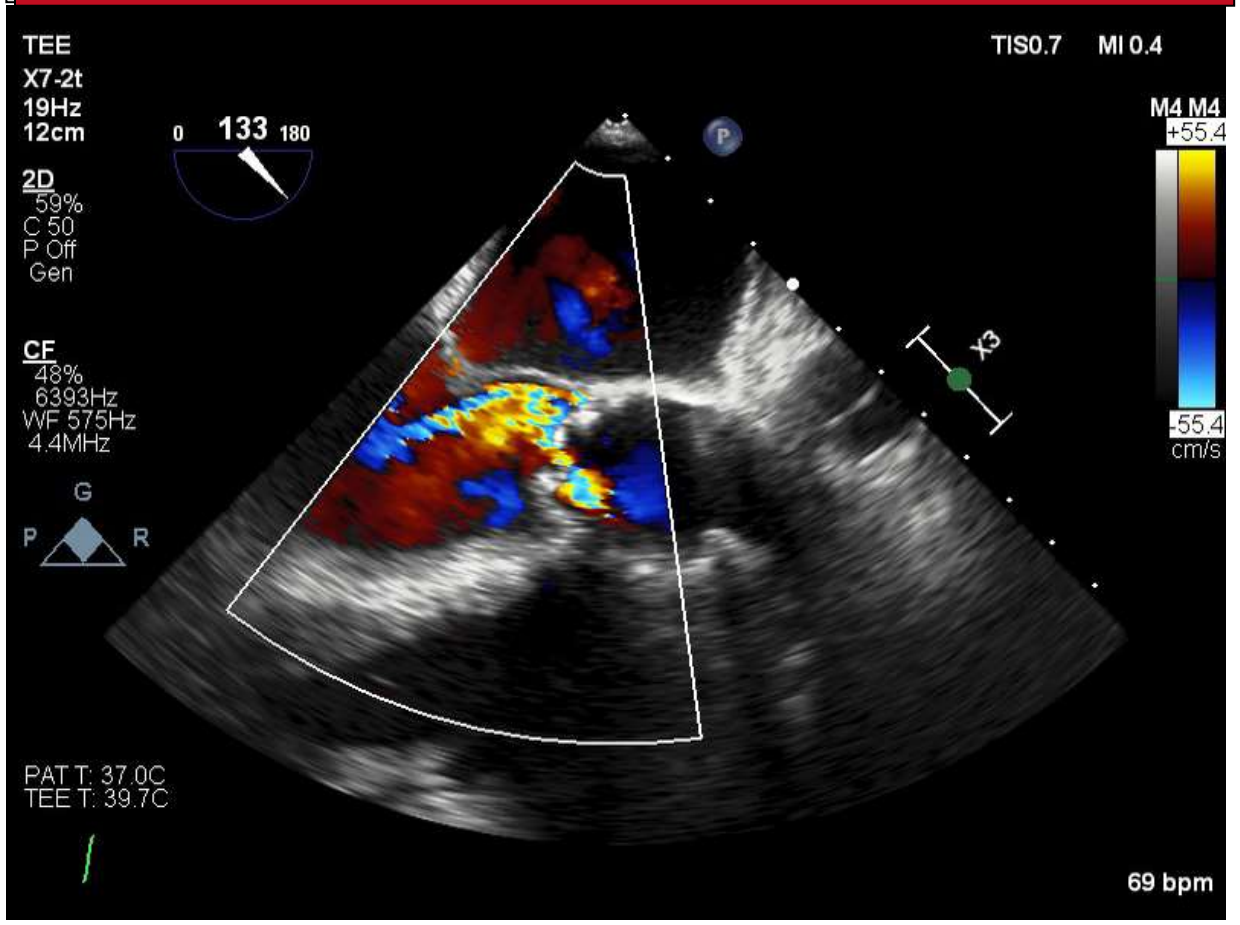
Using IVUS, we confirmed wire position in the true lumen

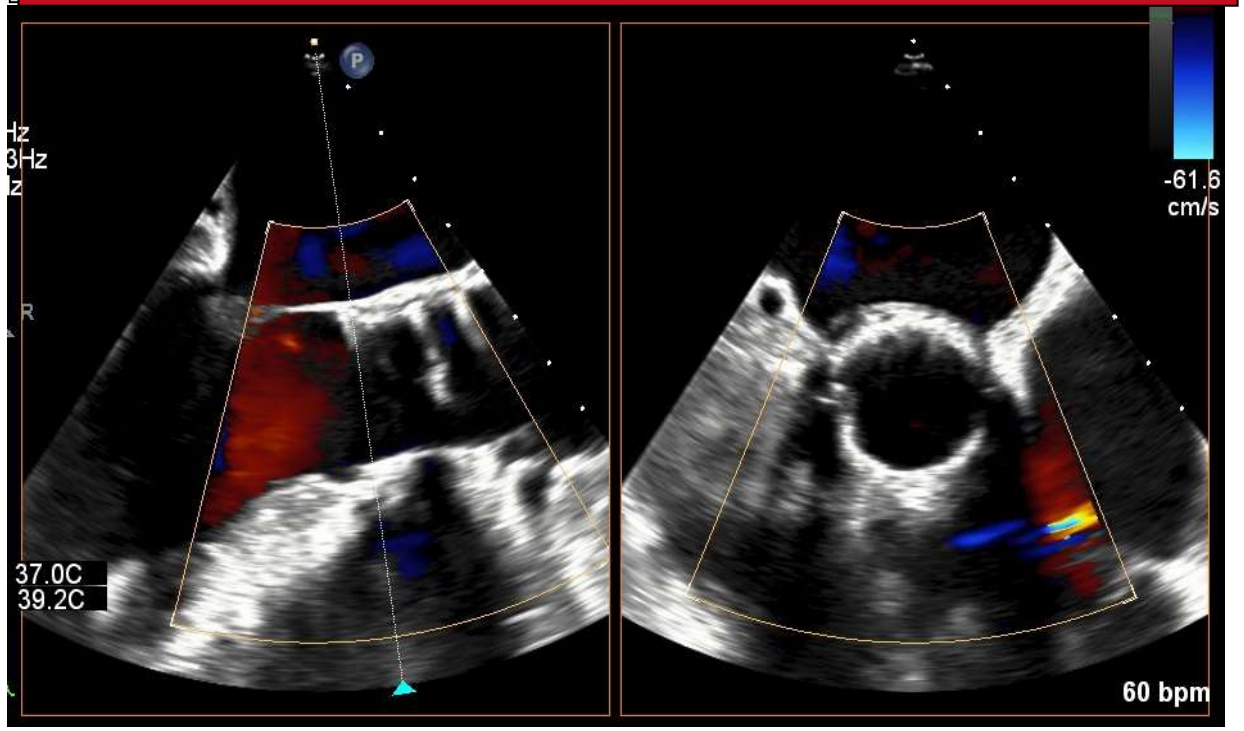
Final Result – No central or PVL

Cedars Sinai
Smidt Heart Institute

Pre-TAVR

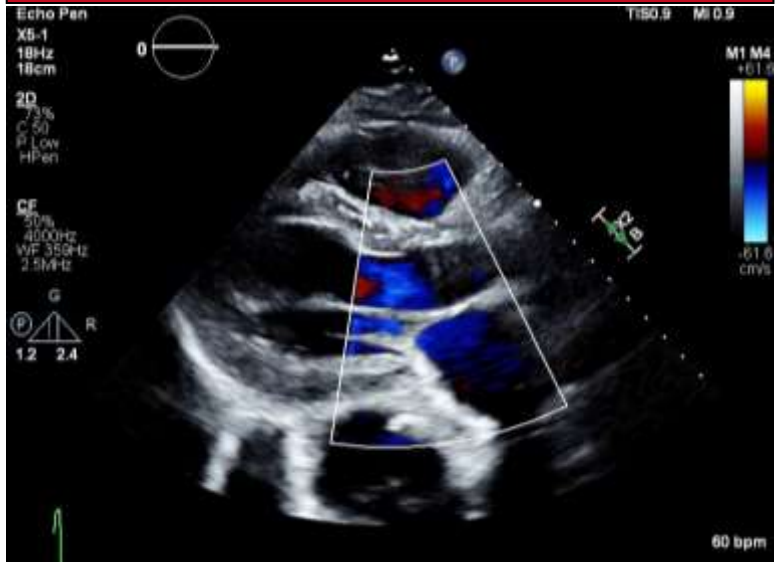
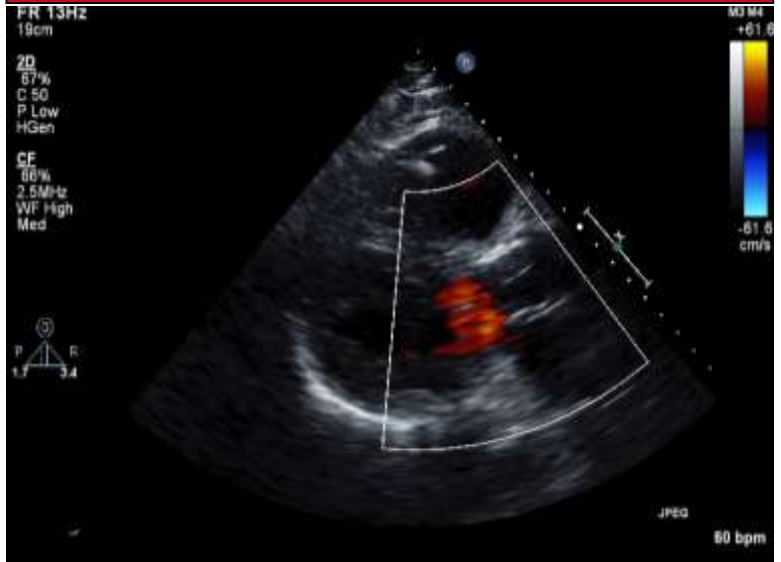
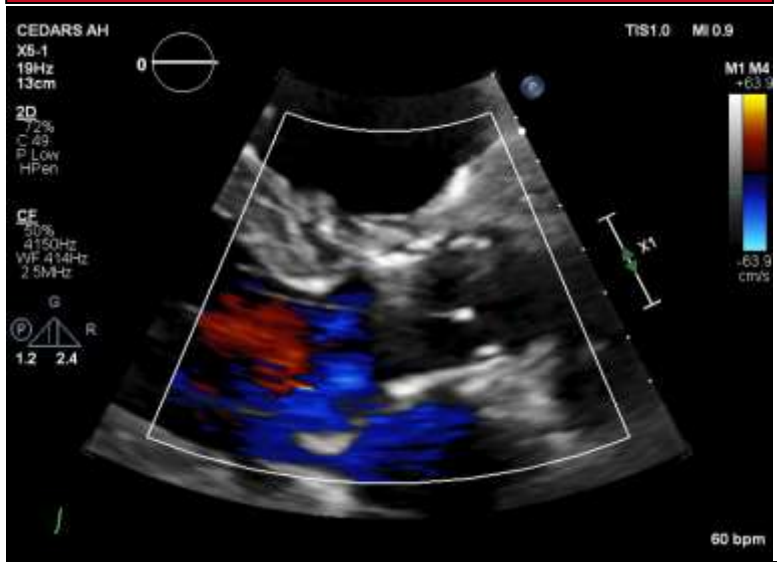
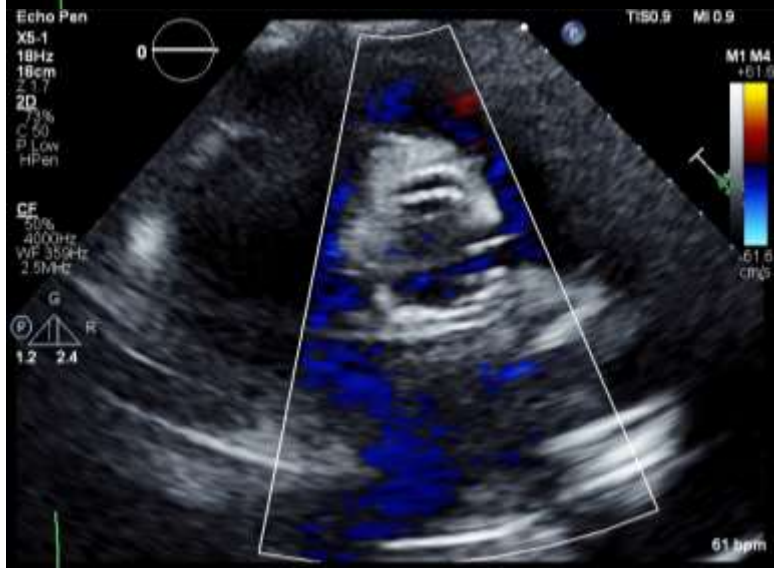
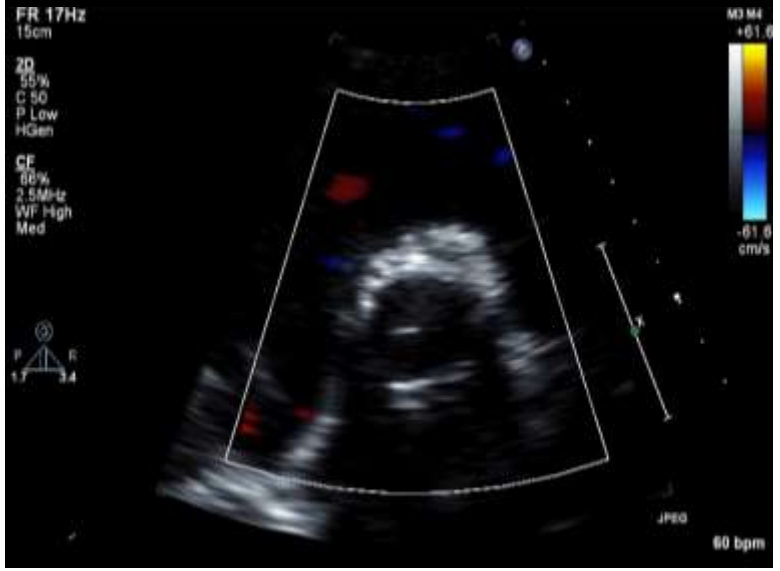
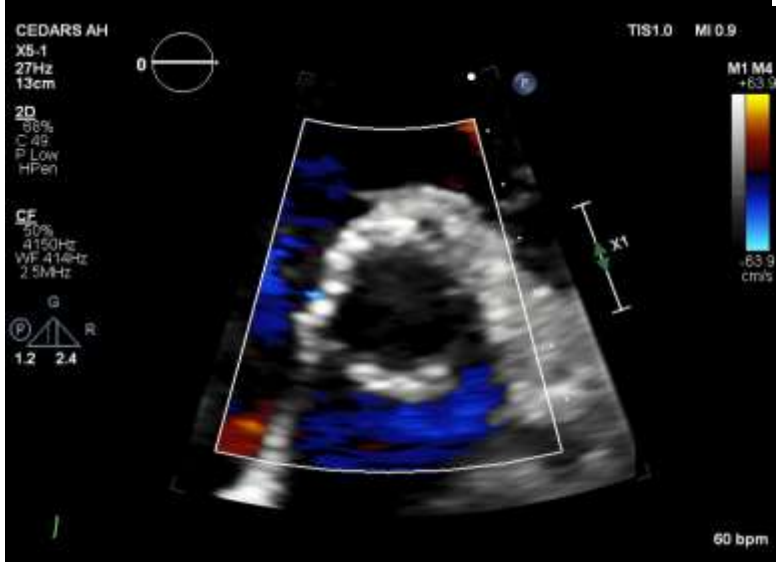


Post-TAVR

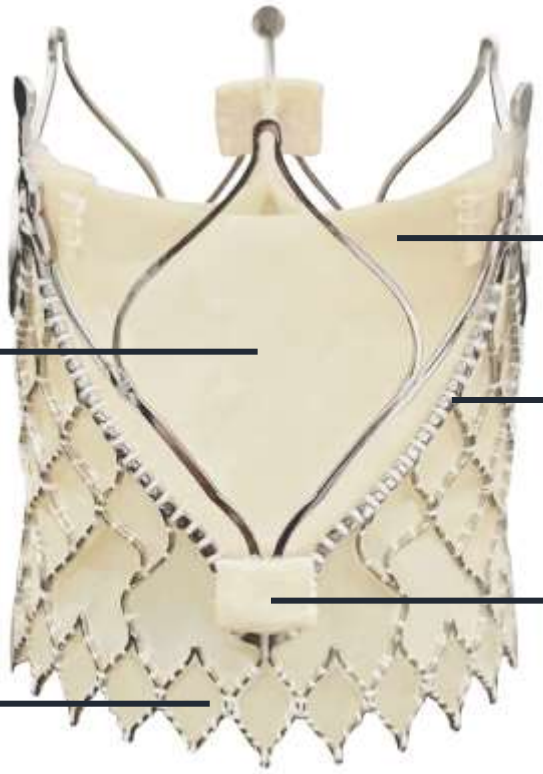


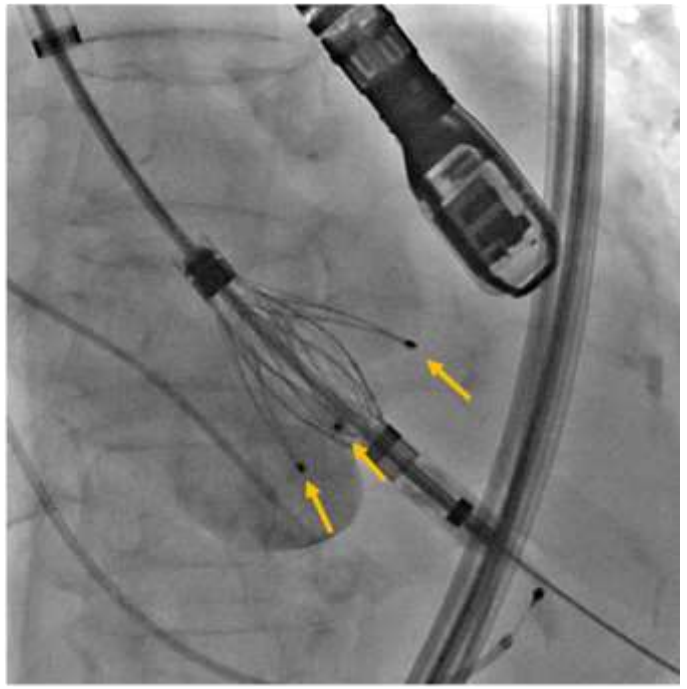
Follow-up with stable gradients and no central or PVL

Cedars Sinai
Smidt Heart Institute

Post-procedure	*1-month*	*1-year*
		
		

The Trilogy™ Heart Valve System





Three Locators Under Fluoroscopy

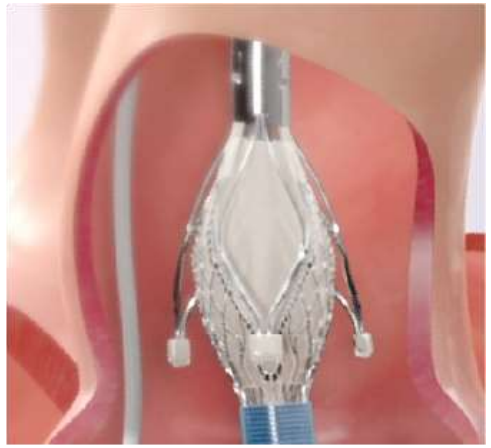
Investigational Use Only – Not for Sale

US: CAUTION – Investigational Device. Limited by Federal (or United States) law to investigational use.

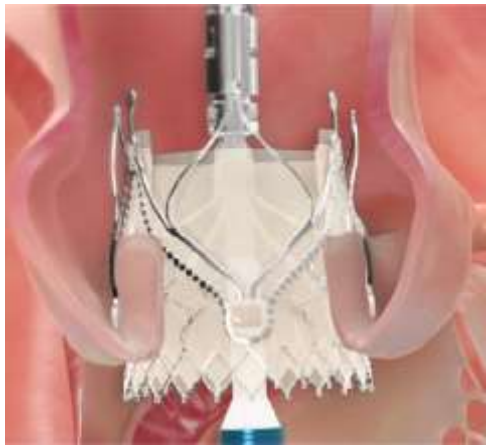
JenaValve Trilogy™ Frame Design with Locator Technology

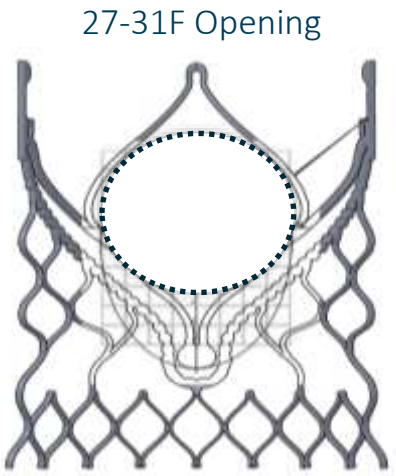
A Unique Design for Securing and Sealing Valve in Native Anatomy

- Aligns THV with Native Cusps
- Locators “Clip” onto Native Leaflets Forming a Natural Seal and Stable Securement

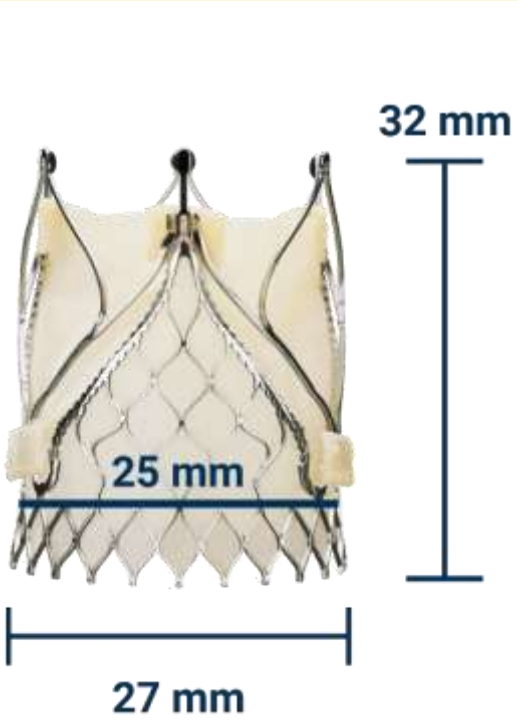
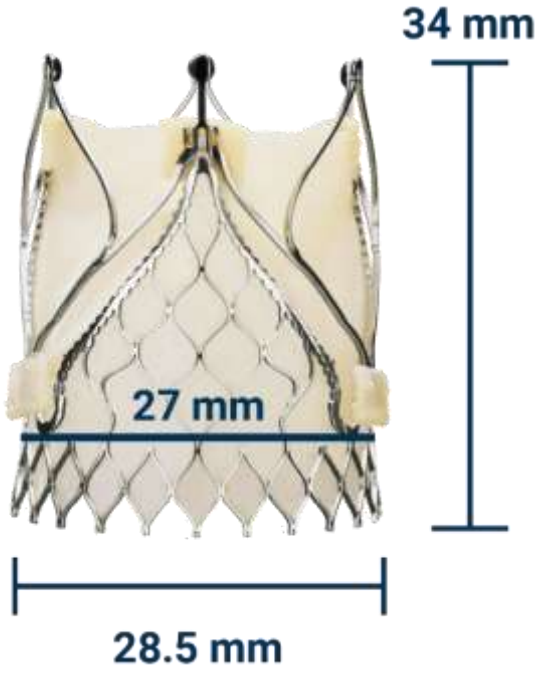


- Large-Open Cells Provides Access to Low Coronaries
- 24 Diamond-Shaped Cells Provide Annular Conformability and Sealing



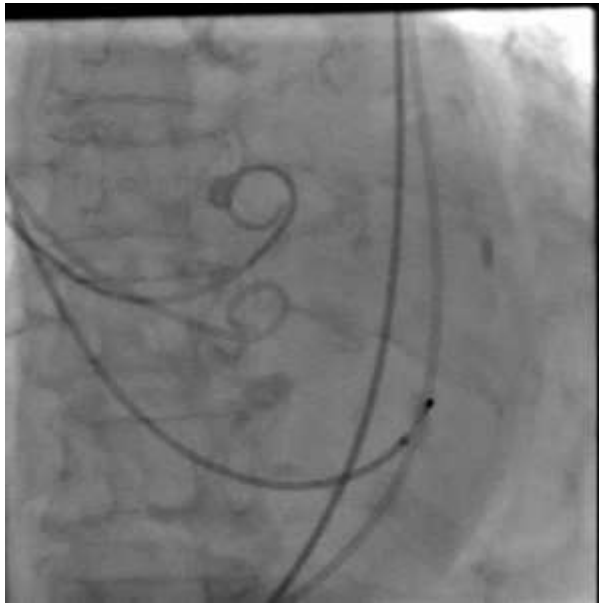


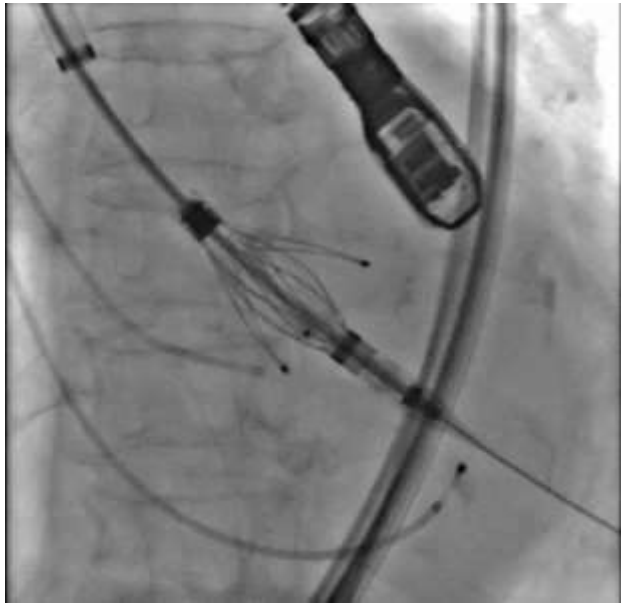
3 sizes

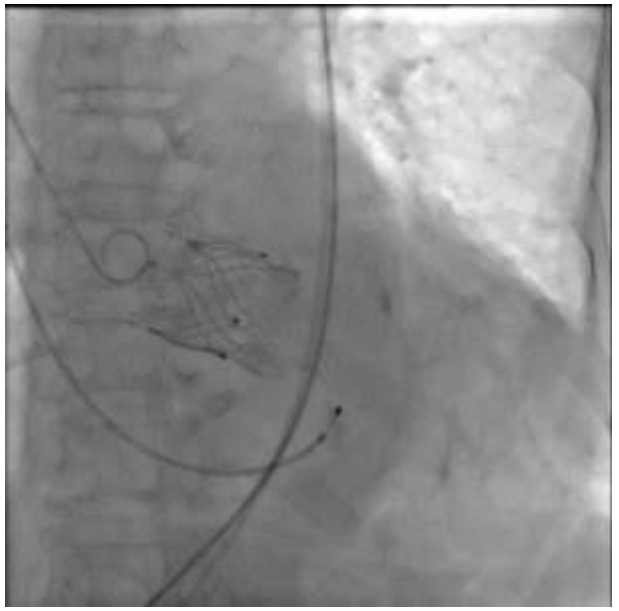
Size 23		Size 25		Size 27	
					
Annular Perimeter Range	66-74 mm	**Annular Perimeter Range**	71-79 mm	**Annular Perimeter Range**	76-85 mm
Annular Diameter Range	21.0-23.6 mm	**Annular Diameter Range**	22.6-25.2 mm	**Annular Diameter Range**	24.2-27.0 mm
Considerations for patients in between sizes: stenotic vs. calcific, LVOT flaring					

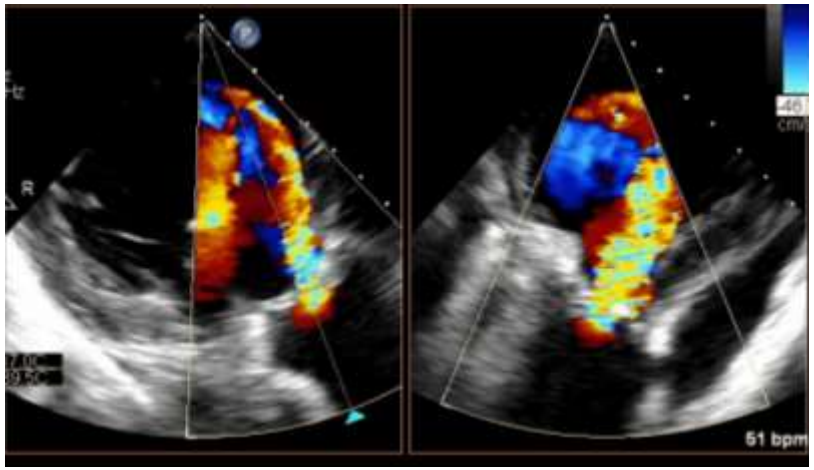
All dimensions are nominal and have been rounded (reference TS-0197.B)
Perimeters derived from annular measurements

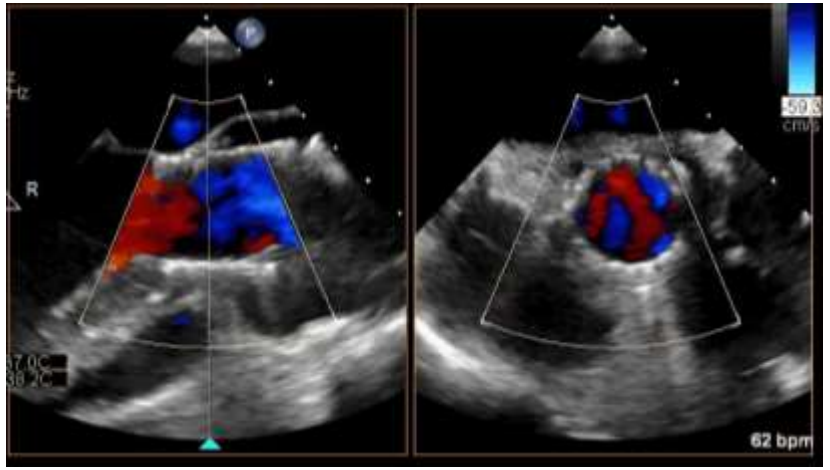
Case Example









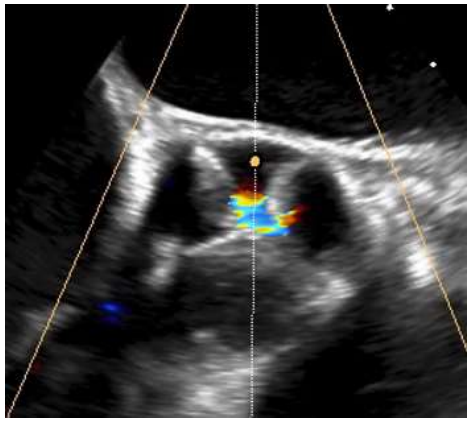


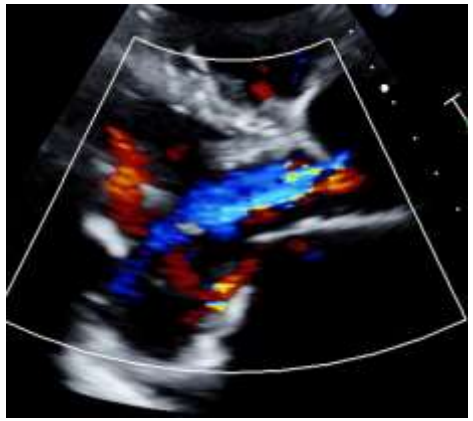
83 y/o female with severe AR due to LVAD

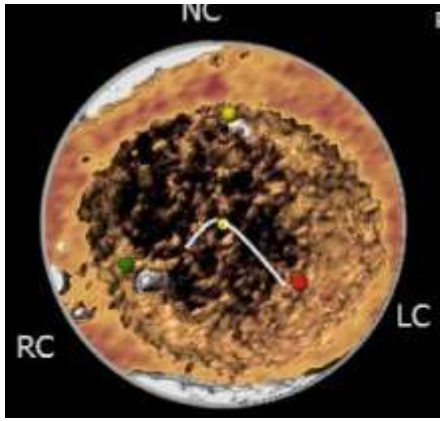
Cedars Sinai
Smidt Heart Institute

- 3 prior sternotomies
- Ischemic Cardiomyopathy, underwent Heartmate II LVAD in 2016

Plan for TAVR with compassionate use of JenaValve Trilogy System



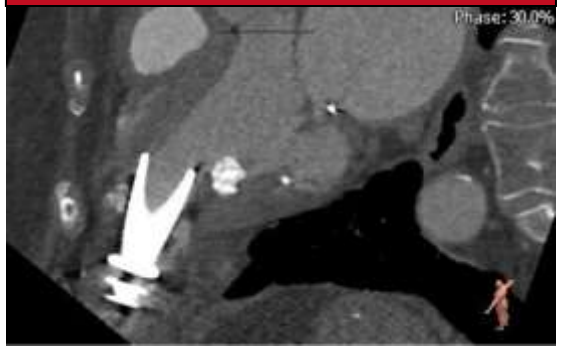


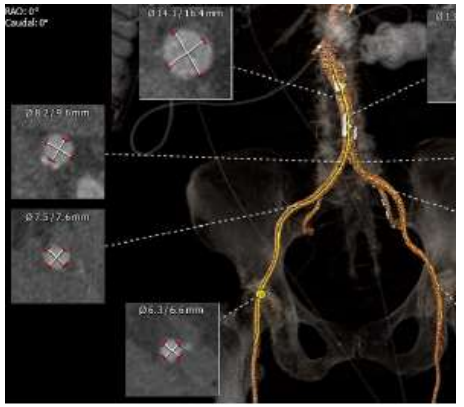


Annulus suitable for 25mm JenaValve

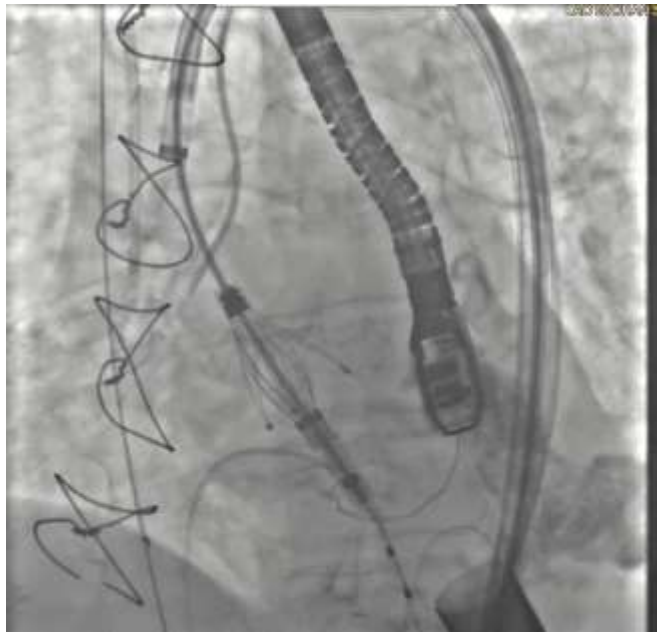
LVOT

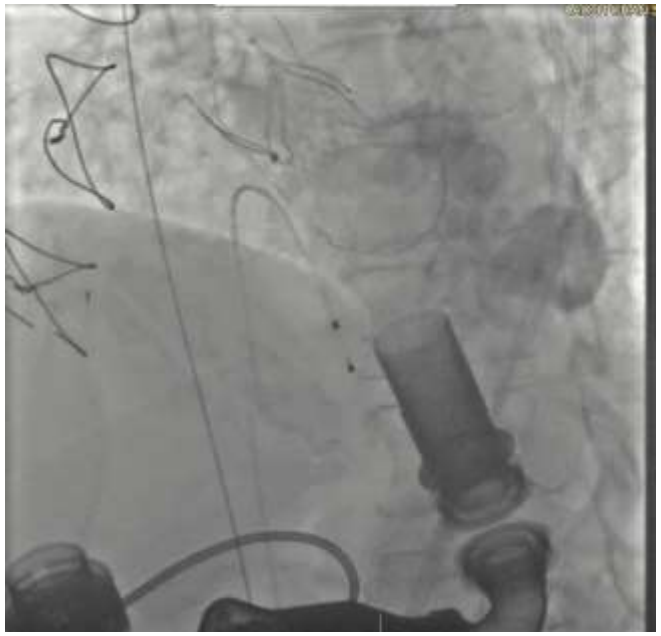
LVAD in place

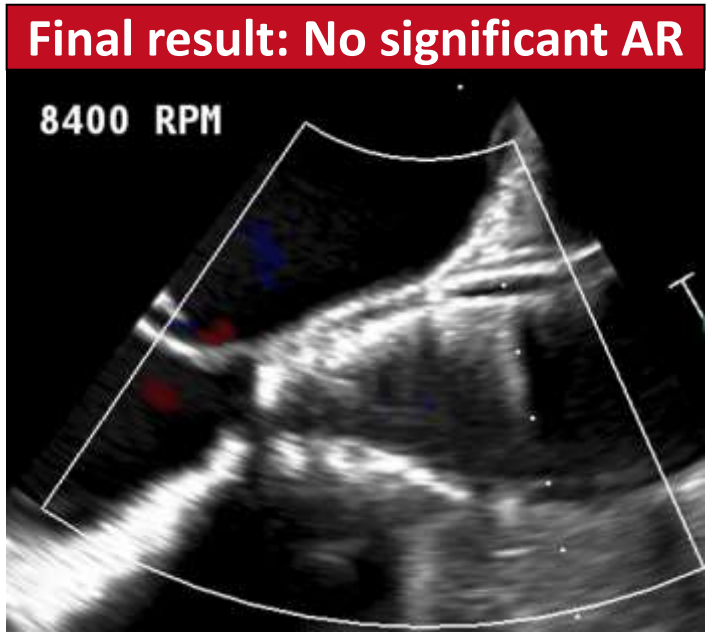




Successful TAVR performed with a 25mm Jena valve





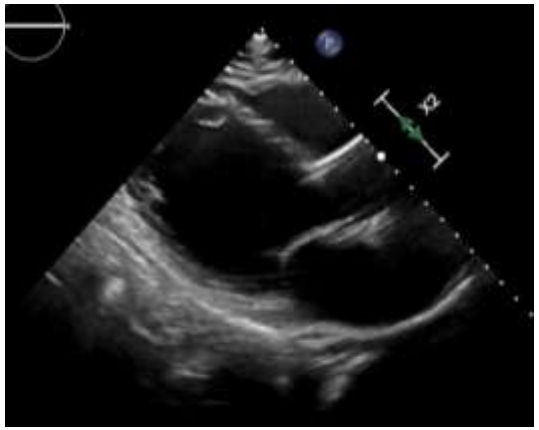


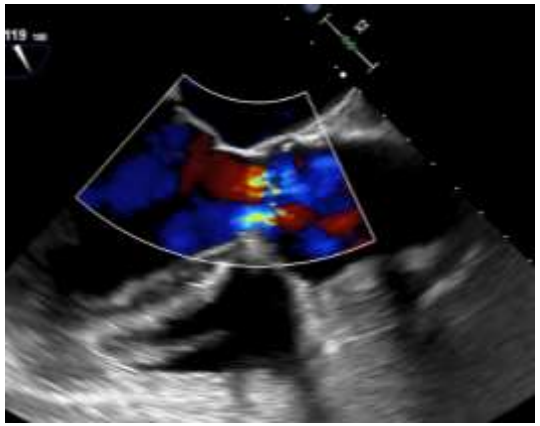
Cedars Sinai
Smidt Heart Institute

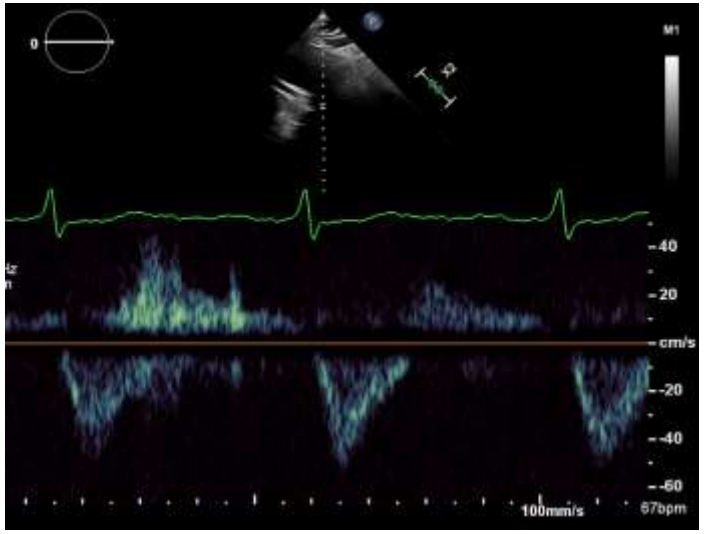
80 y/o male with severe AR

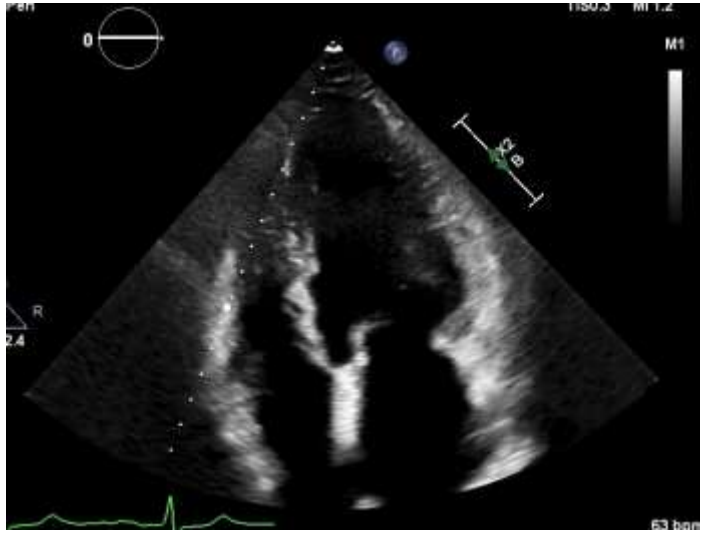
- Ascending aortic aneurysm repair with endograft (2012)
- Aortic valve repair (2012)
- Descending and abdominal aortic aneurysm repair with Dacron graft (2020)

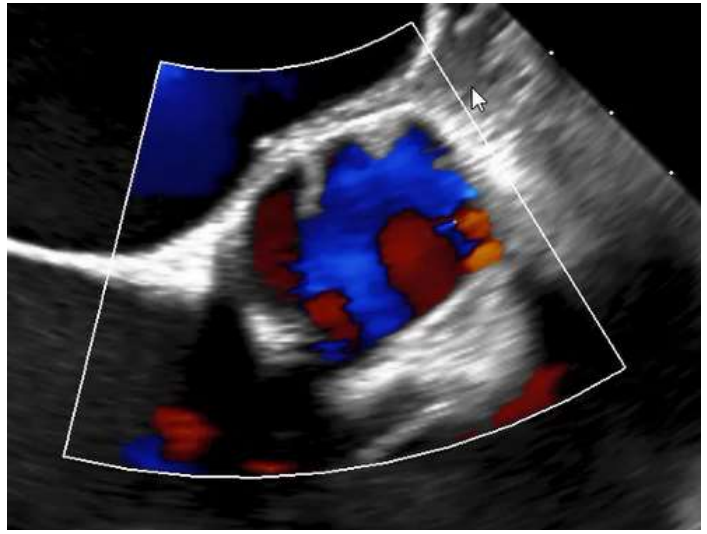
Plan for TAVR with the JenaValve Trilogy System







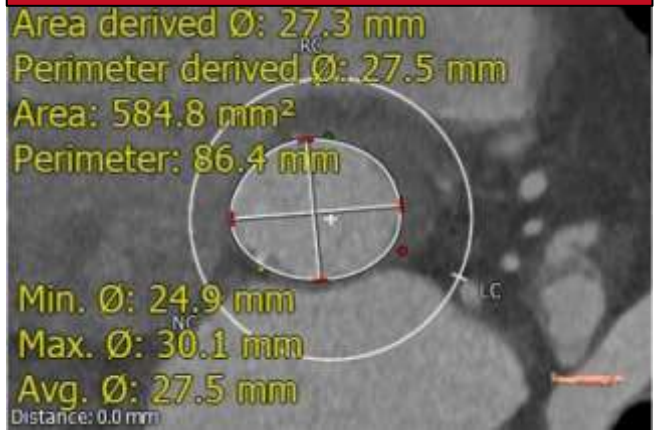




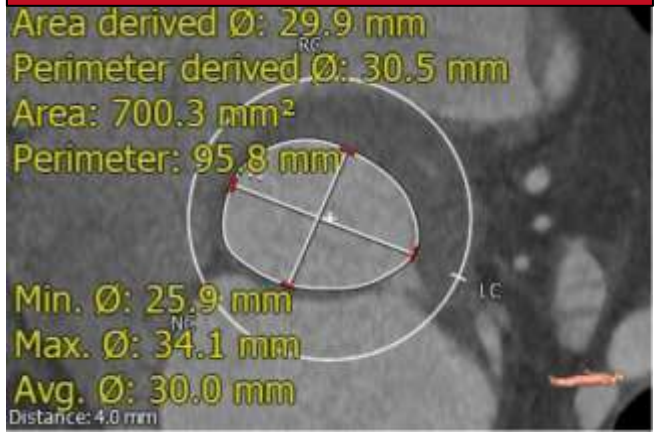
No aortic valve calcium

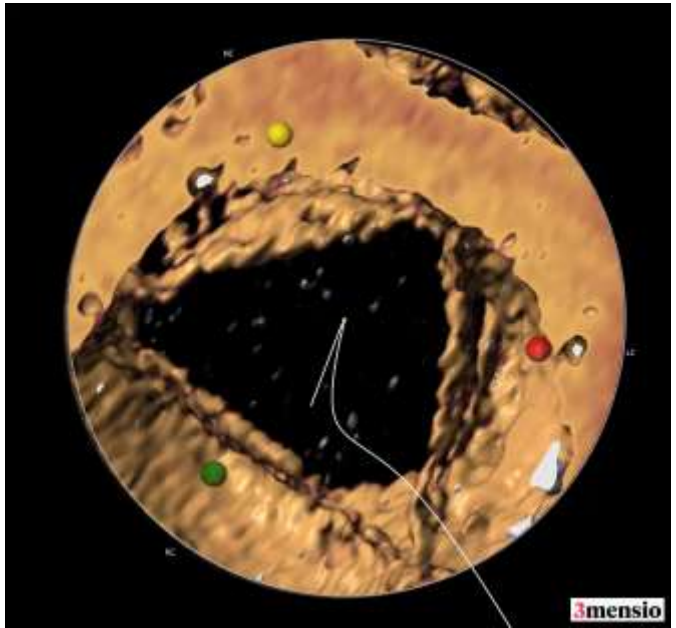
Cedars Sinai
Smidt Heart Institute

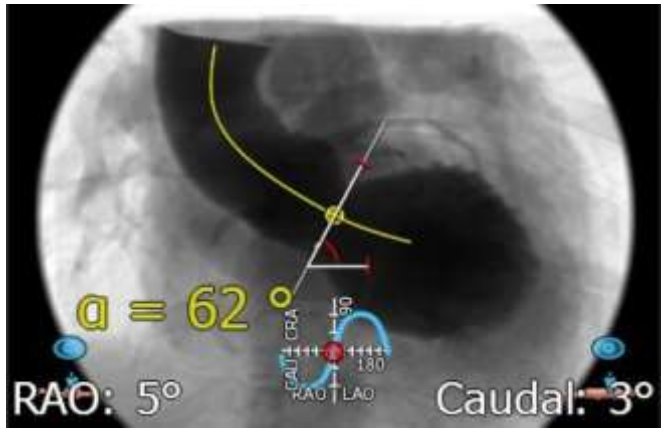
Annulus area 584mm2



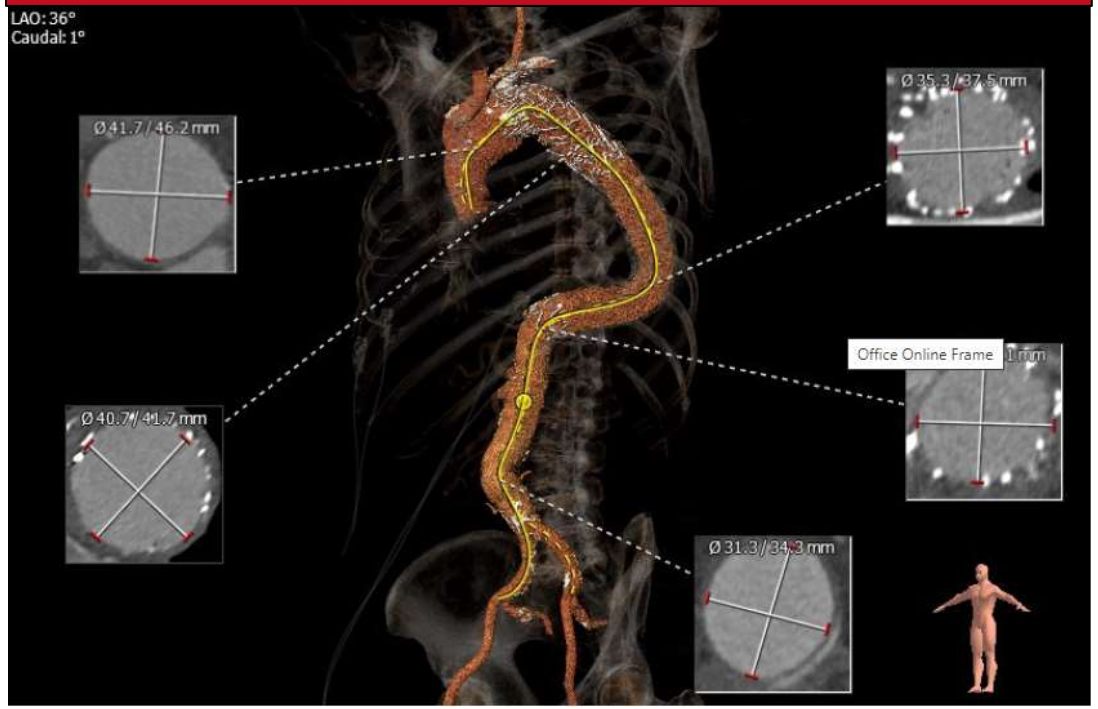
LVOT area 700mm2



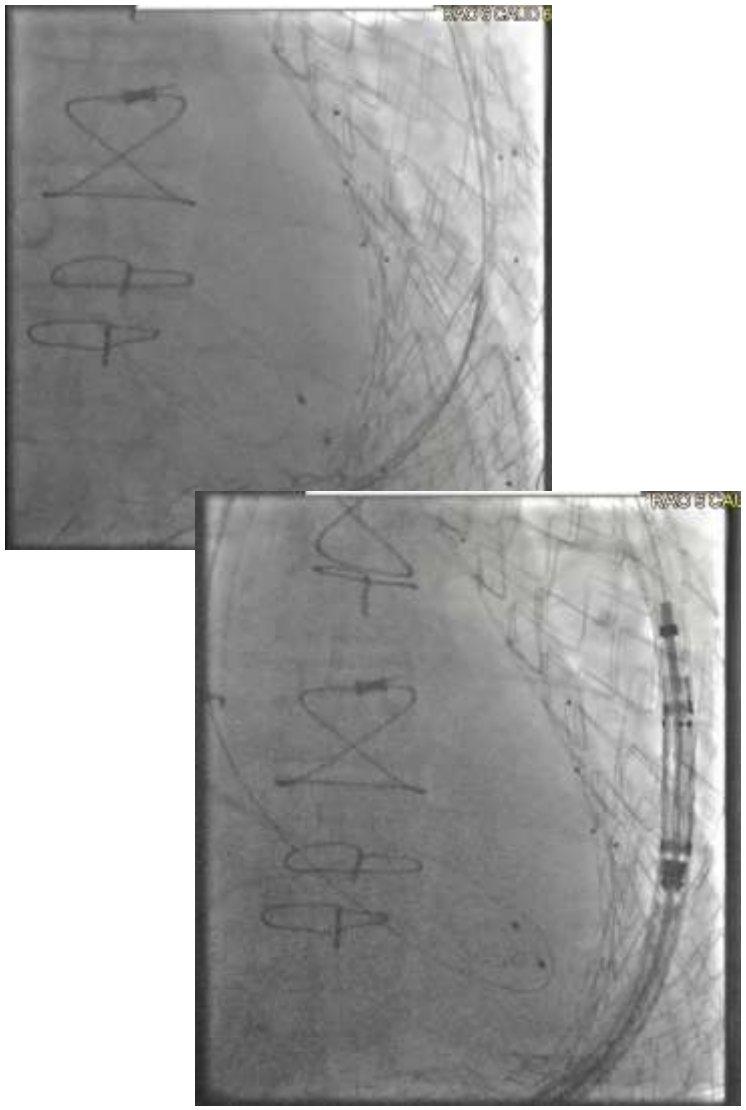


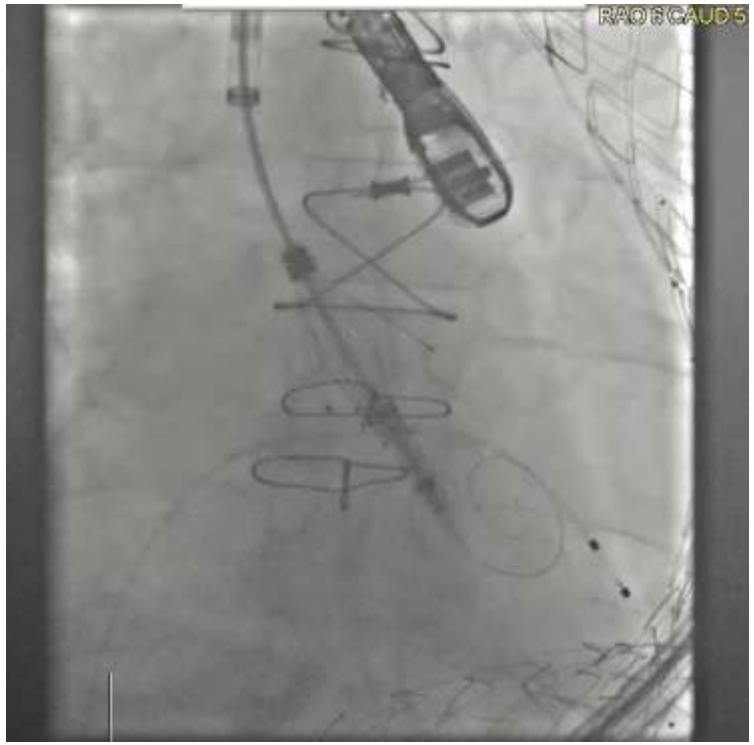


Thoracic aortic endograft

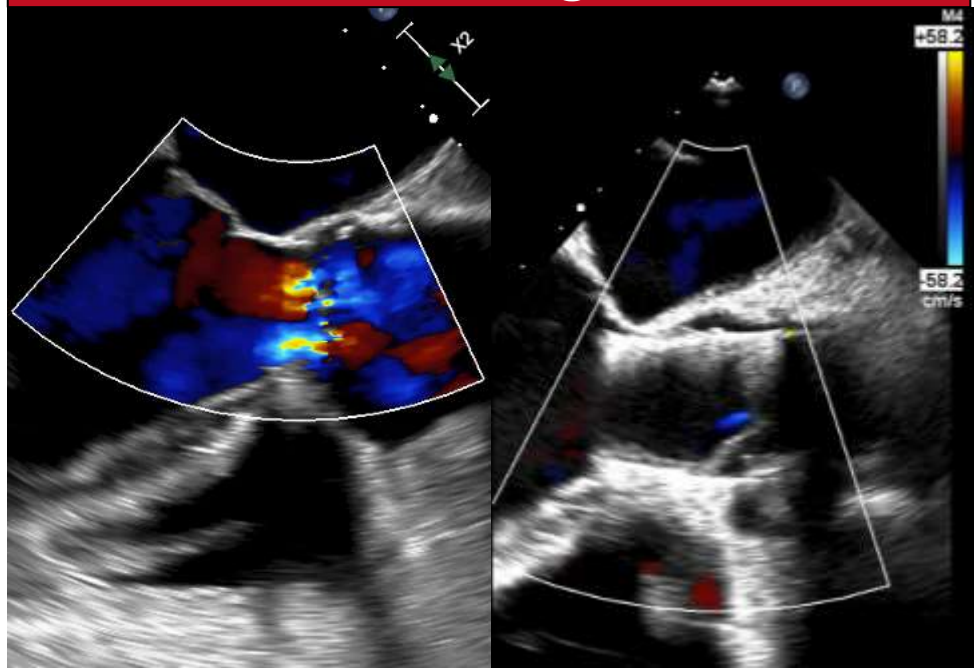


Successful TAVR performed with a 27mm Jena valve



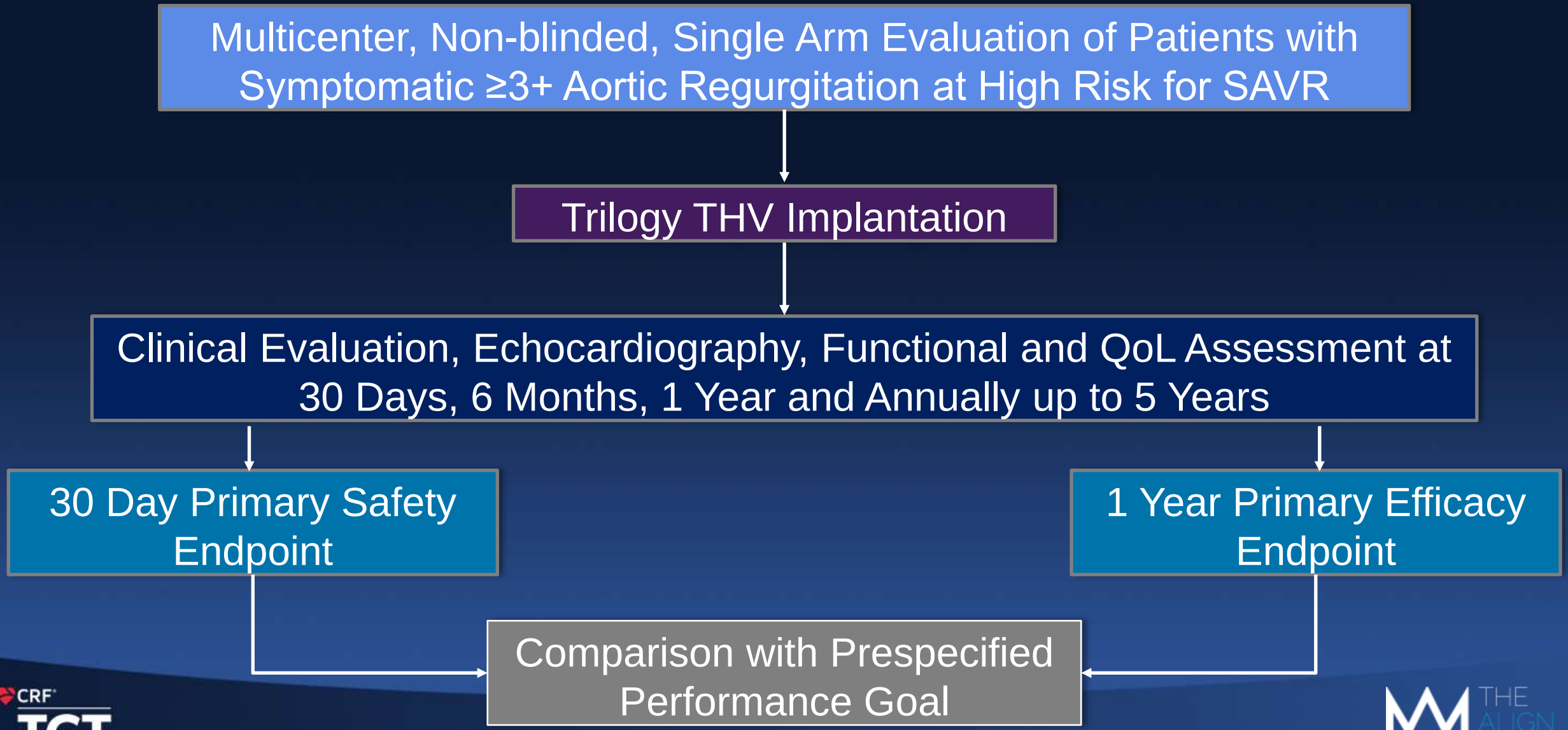


Final result: No significant AR



Cedars Sinai
Smidt Heart Institute

ALIGN AR Study Design

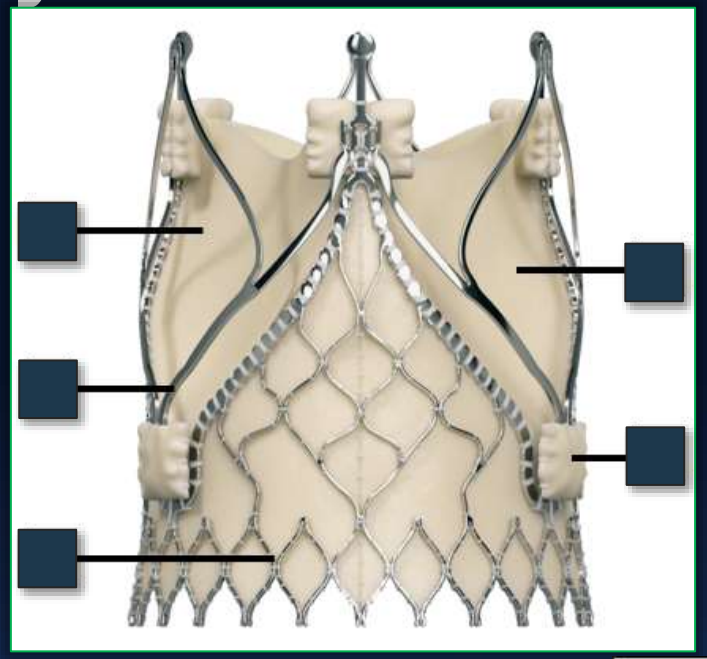


Trilogy THV System for Aortic Regurgitation

27-31 French Open Cell

Nitinol Frame

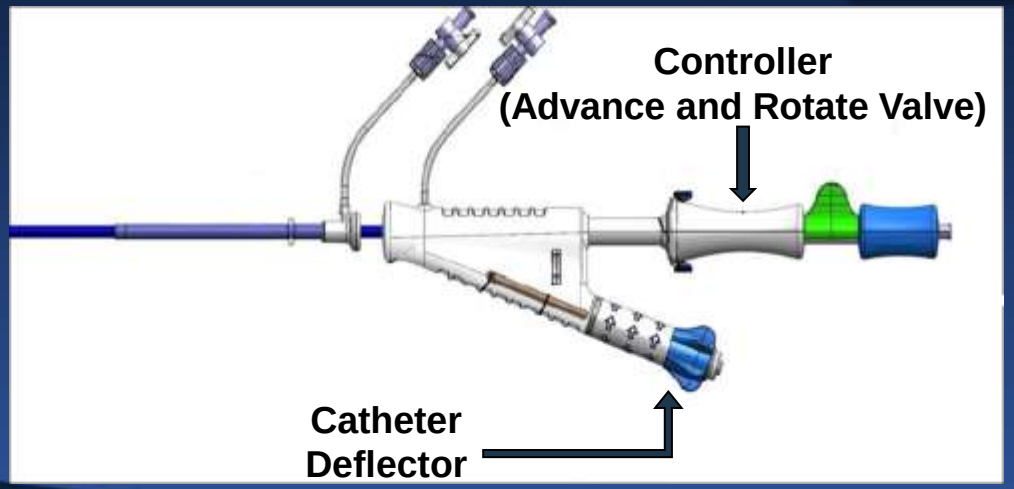
Flared Sealing Skirt

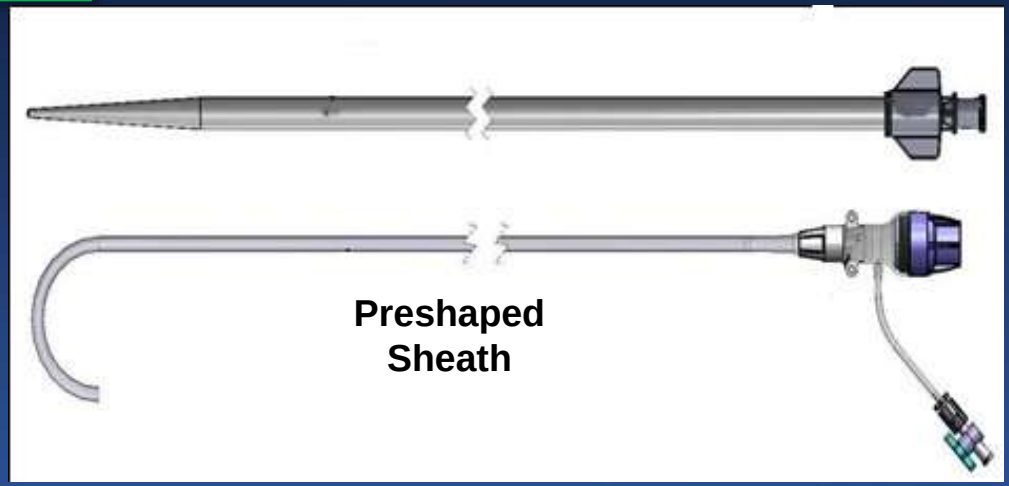


Porcine Pericardial Tissue

Locator

Available in 3 sizes with a perimeter range from 66-90mm





Study Organization

	Investigator	Institution
Study Chair	Martin Leon, MD	Columbia University Medical Center
National Principal Investigators	Vinod Thourani, MD	Piedmont Heart Institute
	Torsten Vahl, MD	Columbia University Medical Center
Executive Steering Committee	Martin Leon, MD	Columbia University Medical Center
	Raj Makkar, MD	Cedars Sinai Medical Center
	Vinod Thourani, MD	Piedmont Heart Institute
	Torsten Vahl, MD	Columbia University Medical Center
	Stephan Baldus, MD	Heart Center Köln
	Hendrik Treede, MD	University Heart and Vascular Center Mainz
CT Core Laboratory	Omar Khalique, MD	Cardiovascular Research Foundation
Echocardiography Core Laboratory	Nadira Hamid, MD	Cardiovascular Research Foundation
DSMB/CEC Chairperson	W. Douglas Weaver, MD	Henry Ford Health System

Key Inclusion and Exclusion Criteria

Inclusion

- Adult patients with moderate to severe or severe (Grade ≥3) AR assessed according to ASE criteria
- NYHA Class II or greater symptoms
- High-risk for SAVR defined by the Heart Team

Exclusion

- Congenital unicuspid or bicuspid aortic valve
- Aortic root diameter >5.0 cm
- Previous prosthetic aortic valve
- Mitral regurgitation >moderate
- CAD requiring revascularization

Primary Endpoints

- **The primary safety endpoint was a composite at 30 days based on VARC-2 definitions**
  - All-cause mortality, any stroke, major vascular complication, life threatening or major bleeding, new pacemaker, acute kidney injury, valve dysfunction and surgery or intervention related to the device
- **The primary efficacy endpoint was all-cause mortality at 12 months**

Primary Safety Endpoint: Performance Goal Derivation

Performance Goal derived from contemporary high-risk AS TAVR trials reporting VARC-2 composite endpoints*
(REPRISE III, PORTICO IDE, SOLVE TAVR, n=1108)

↓

Weighted Safety Composite Endpoint = 30.0%
Performance Goal Margin = 1.35

↓

Performance Goal for 30-Day Composite Safety Endpoint = 40.5%

*Only the FDA or CE approved device cohorts were included in weighted composite endpoint derivation (investigational device cohorts excluded)

Primary Efficacy Endpoint: Performance Goal Derivation

Performance Goal for efficacy derived as a weighted average of 1-year mortality with conservative management according to NYHA Class

Class I/II		Class III/IV		Weighted Average
19.1% x 30%	+	34.7% x 70%	=	30.0%

Literature for conservative treatment of ssAR is limited, so weighted average reduced from 30% by 5%

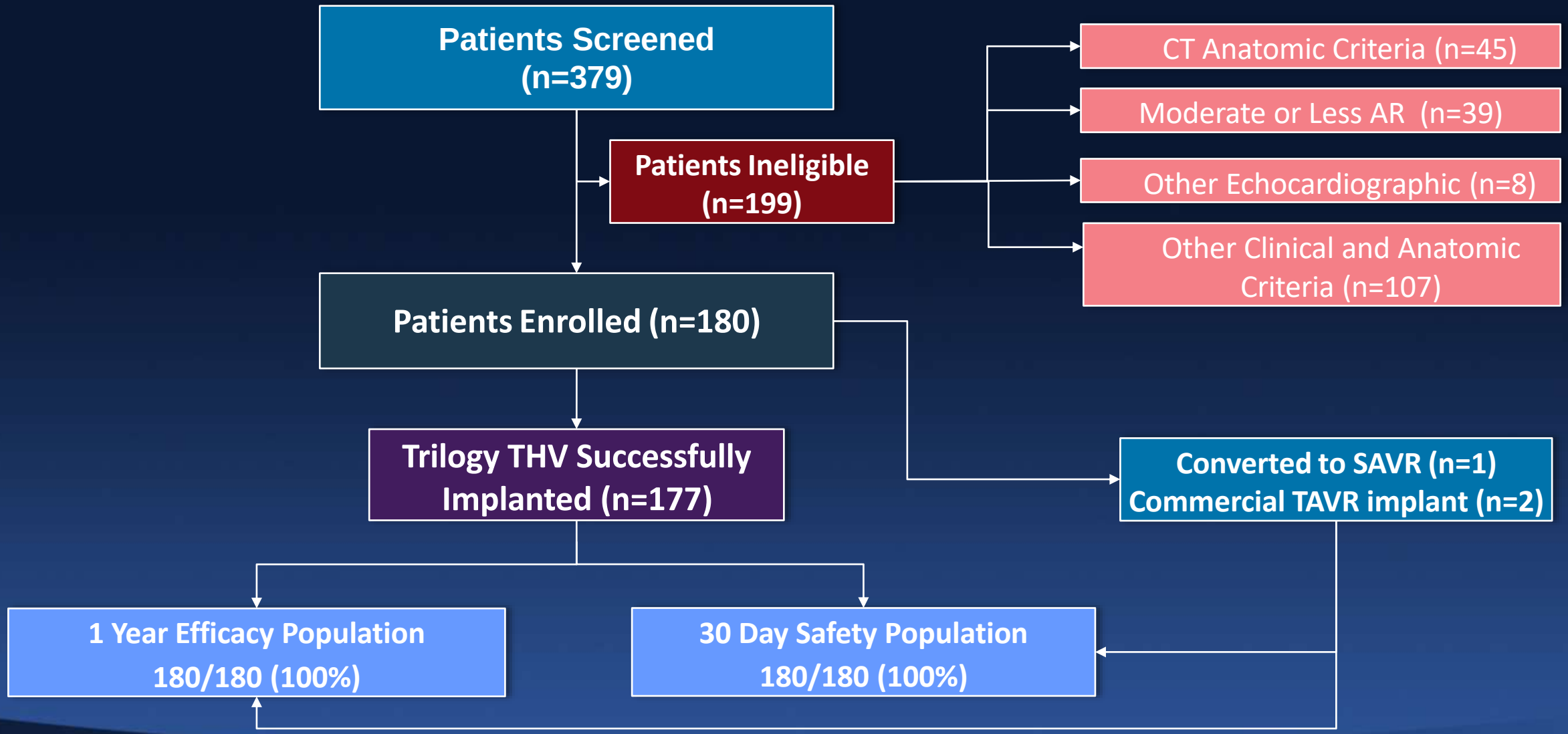
Performance Goal for 1-Year Primary Efficacy Endpoint = 25.0%

Turk et al. *Ann Thorac Surg*. 2010;89:731-7.
Sampat et al. *J Am Coll Cardiol*.2009;54:452-7.
Fiedler et al. *Heart*. 2018;104:835-40.
Kamath et al. *Circulation*.2009;120:S134-8.

Study Methodology

- The primary safety and efficacy endpoints are compared for noninferiority against the prespecified performance goals using the one tailed z-test with an $\alpha = 0.025$
- Each patient reviewed (including imaging studies) and accepted by multi-disciplinary Heart Team AND unanimous vote of case review board
- Core lab review of all cardiac imaging
- 100% CEC adjudication of all major events using applicable VARC-2 definitions
- 5-year clinical and echocardiography follow-up planned in all patients

Screening and Patient Disposition (As Treated)



Baseline Patient Characteristics

Demographics and Co-Morbidities		Vascular & Other Co-Morbidities	
Age (years)	75.5 ± 10.8	Atrial Fibrillation	40.6%
Female	47.2%	Pulmonary Hypertension	25.6%
BMI – kg/m^2	25.3 ± 6.1	Prior Permanent Pacemaker	16.1%
STS Score	4.1 ± 3.4	Left Bundle Branch Block	5.6%
NYHA Class III or IV	67.2%	Right Bundle Branch Block	10.6%
Hypertension	82.8%	Prior CABG	11.1%
Diabetes	14.5%	Prior PCI	20.6%
Renal Insufficiency	32.2%	Prior CVA	10.6%
Frailty	33.9%	Carotid Disease	10.0%
Prior Endocarditis	11.7%	Peripheral Arterial Disease	17.8%

Baseline Patient Characteristics

Demographics and Co-Morbidities		Vascular & Other Co-Morbidities	
Age (years)	75.5 ± 10.8	Atrial Fibrillation	40.6%
Female	47.2%	Pulmonary Hypertension	25.6%
BMI – kg/m^2	25.3 ± 6.1	Prior Permanent Pacemaker	16.1%
STS Score	4.1 ± 3.4	Left Bundle Branch Block	5.6%
NYHA Class III or IV	67.2%	Right Bundle Branch Block	10.6%
Hypertension	82.8%	Prior CABG	11.1%
Diabetes	14.5%	Prior PCI	20.6%
Renal Insufficiency	32.2%	Prior CVA	10.6%
Frailty	33.9%	Carotid Disease	10.0%
Prior Endocarditis	11.7%	Peripheral Arterial Disease	17.8%

ALIGN AR Patient Population

- 77 patients (42.7%) 80+ years with average STS 4.3%
- 36 patients (20.0%) 85+ years with average STS 4.6%
- 33.9% Classified as Frail
  - 116 patients (64.4%) with 1+ Frailty measure (6MWT, Grip, Katz, BMI <20)
  - 44 patients (24.4%) with 2+ Frailty measures
    - 89 if include Hgb below threshold (49.4%)

Baseline Imaging Characteristics

	%(n) or mean ± SD		mean ± SD
AR Severity		Regurgitant Volume (ml)	55.5 ± 17.2
Severe	64.4% (116)		
Moderate to Severe	31.7% (57)	LVESD (mm)	39.6 ± 10.2
Moderate	2.8% (5)		
Not Evaluable	1.1% (2)	LVESV (ml)	70.6 ± 38.9
Vena Contracta Width	0.7 +/- 0.1	LVEF (% ± SD)	53.8 ± 11.4
Prominent Holodiastolic Flow	46.7% (84)	LV Mass Index (g/m^2)	172.7 ± 61.8
Mean Gradient (mmHg)	8.7 ± 6.6	CT – Annulus Perimeter (mm)	78.7 ± 8.9
Regurgitant Fraction (%)	55.3 ± 12.9	CT – Annulus Area (mm^2)	480.1 ± 101.4

Procedural Details

Variable	% (n)
General Anesthesia	91.1%, (164)
Procedure Time	71.8± 24.9 min
Contrast Volume	110.0 ± 54.9 cc
Post-BAV Dilatation	3.9% (7)
Trilogy Valve Implanted Large Medium Small	 57.2% (103) 20.0% (36) 22.8% (41)

Procedural Outcomes

Outcome	% (n)
In-procedural Death	0
Annular Rupture	0
Ventricular Perforation	0
Coronary Obstruction	0
Valve Embolization	2.2% (4)
Aortic Dissection	0.6% (1)
Femoral Access Site Intervention	2.2% (4)
Success	
Technical Success	95.0% (171)
Device Success	96.7% (174)
Procedure Success	92.8% (167)

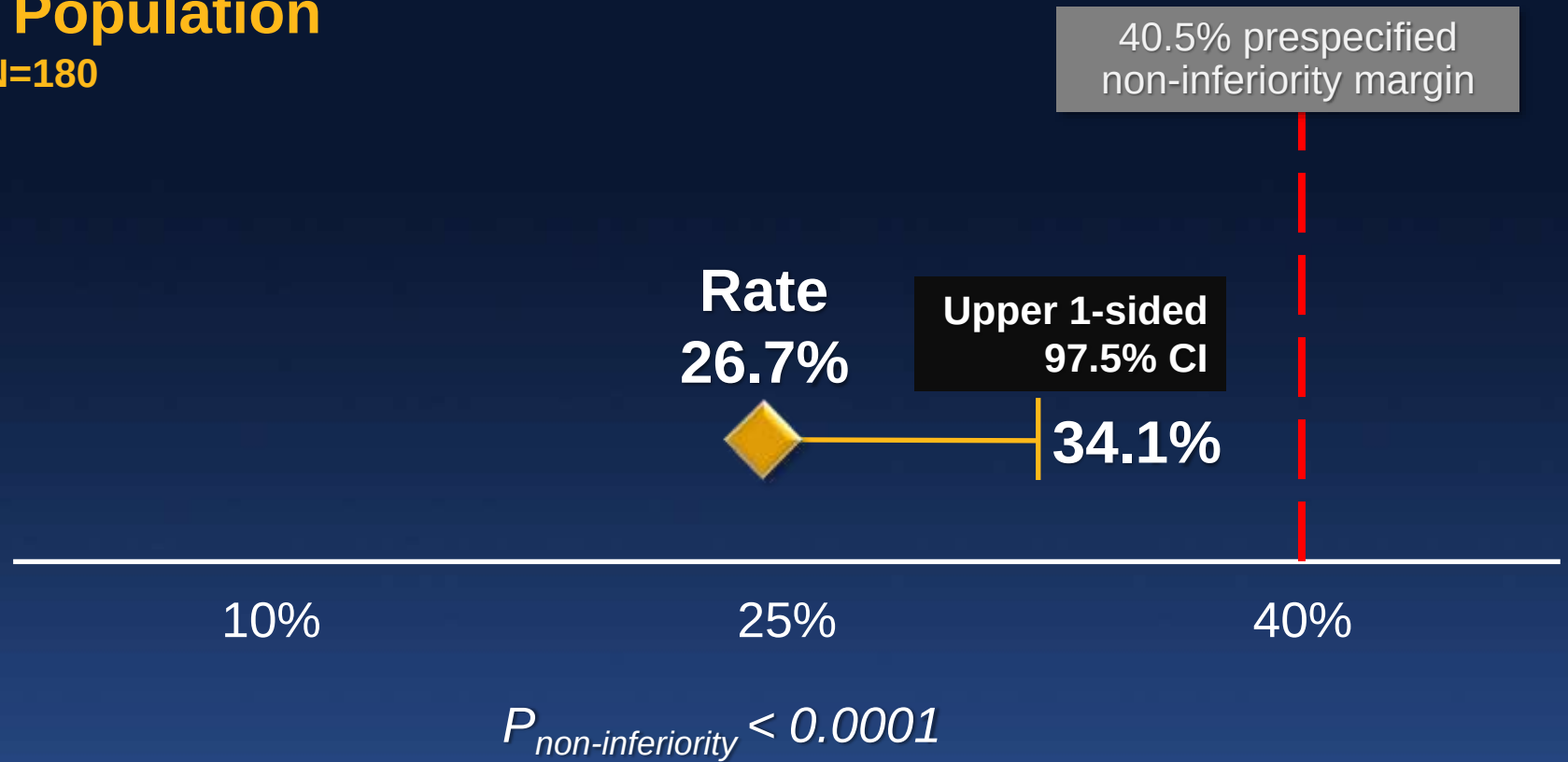
Primary Safety Endpoint at 30 Days

Variable	% (n)
All Cause Mortality	2.2% (4)
Cardiovascular Mortality	2.2% (4)
Any Stroke Disabling Stroke Nondisabling Stroke	2.2% (4) 1.1% (2) 1.1% (2)
Major/Life Threatening Bleeding	4.4% (8)
Major Vascular Complication	3.9% (7)
Acute Kidney Injury Stage 2 or 3 or Dialysis (7 Days)	1.1% (2)
Surgery/Intervention Related to the Device	2.8% (5)
New Pacemaker Implantation Pre-existing PPM	24.0% (36) 16.7% (30)
≥ Moderate Paravalvular Regurgitation	0.6% (1)
Total	26.7% (48)

Primary Safety Endpoint at 30 Days*

Enrolled Population

N=180



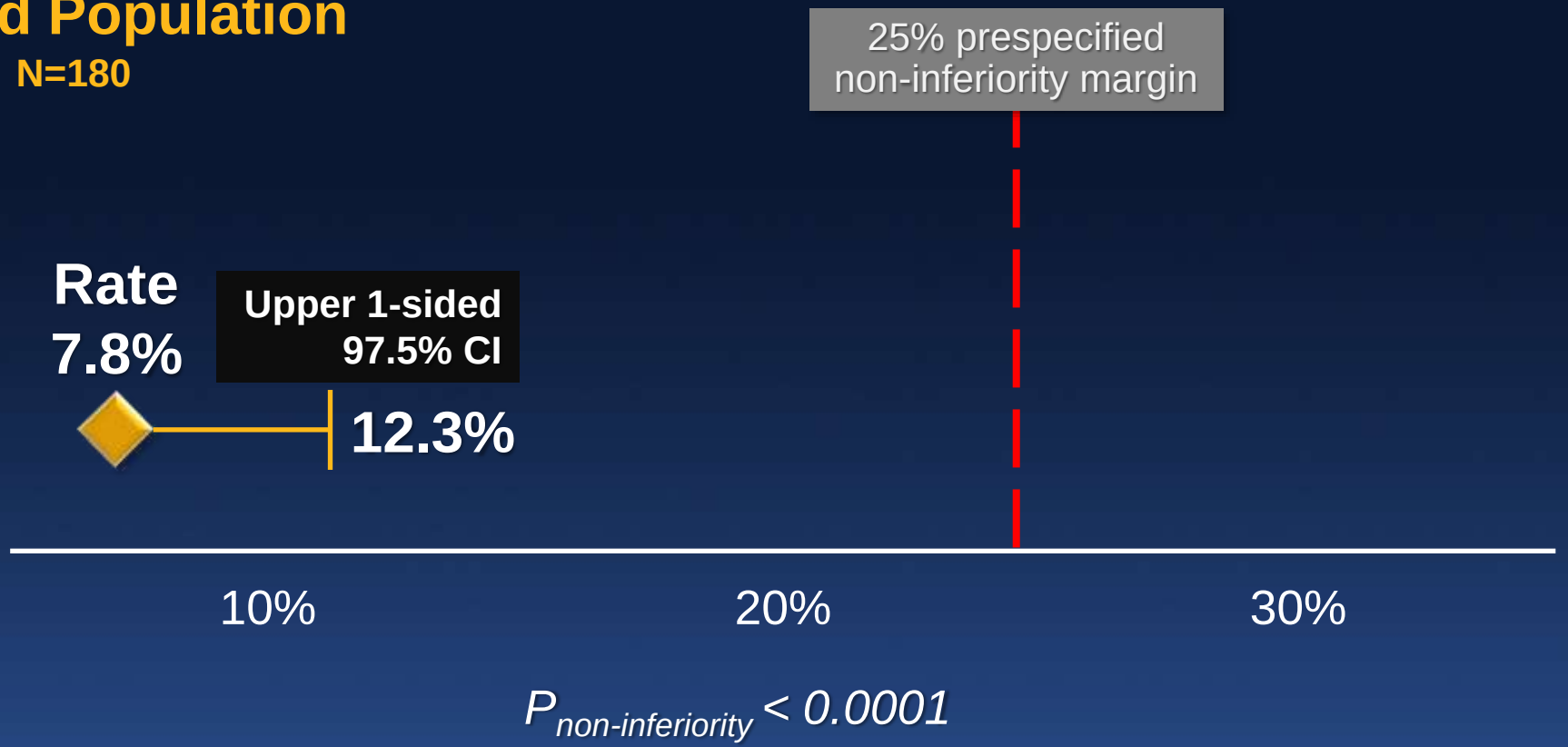
$P_{non\text{-}inferiority} < 0.0001$

Non-inferiority criteria met for primary safety endpoint

*Composite of 30 day all-cause mortality, all stroke, life-threatening/major bleeding, major vascular complications, AKI ≥ 2 or dialysis, valve intervention, new permanent pacemaker, ≥ moderate PVR

Primary Efficacy Endpoint at 1 Year*

Enrolled Population
N=180

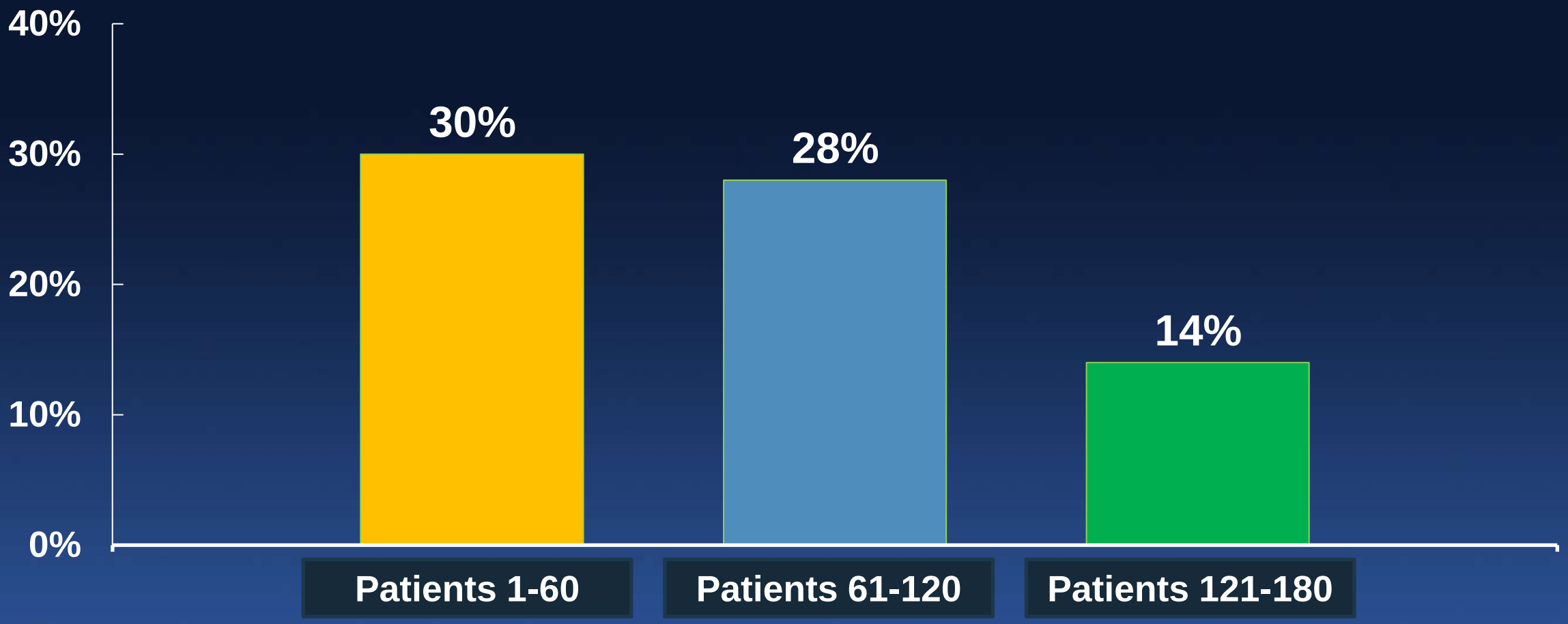


$P_{non\text{-}inferiority} < 0.0001$

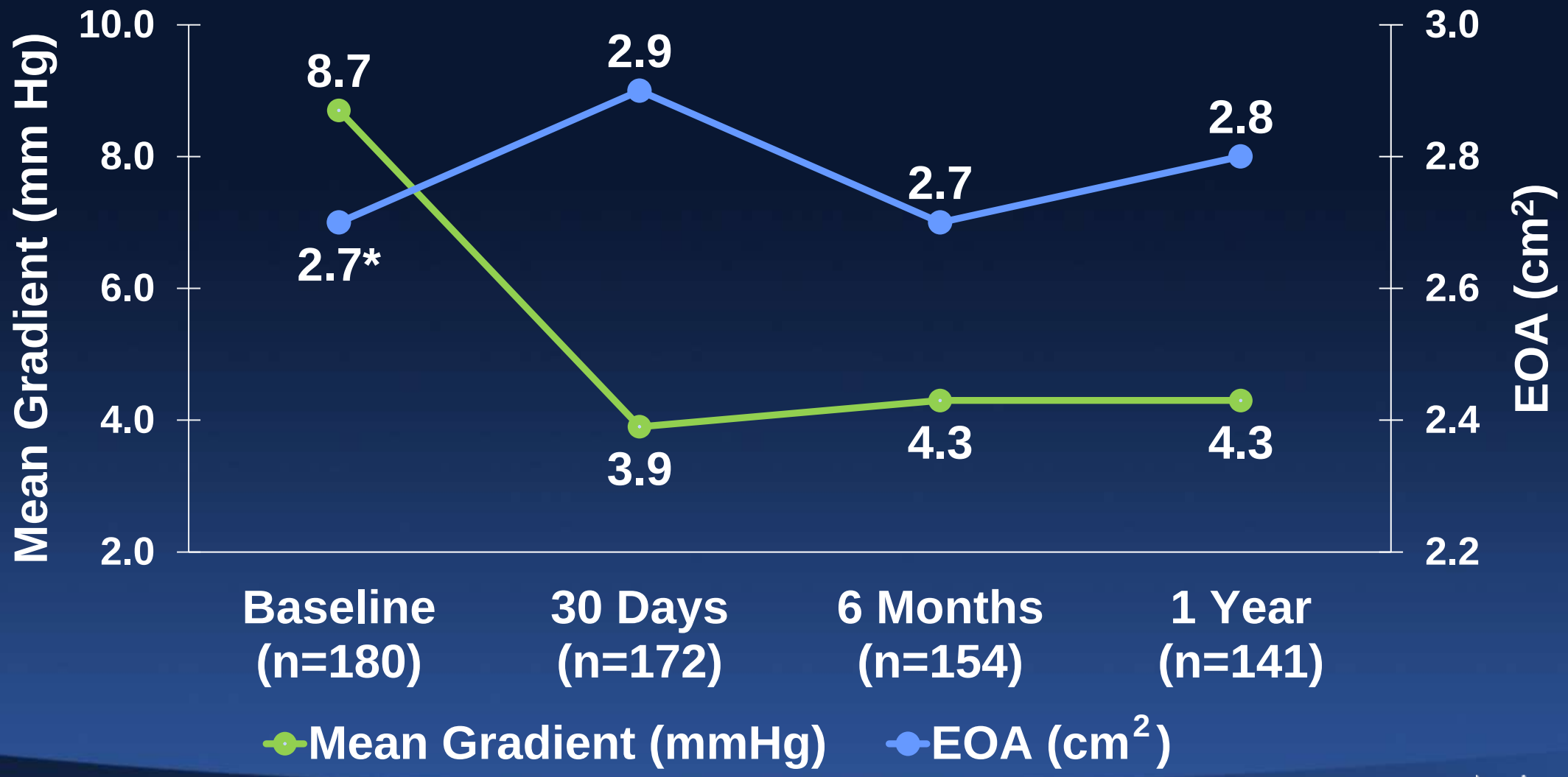
Non-inferiority criteria met for primary efficacy endpoint

*All-cause mortality

New Pacemaker Implant Rate By Tercile of Enrollment

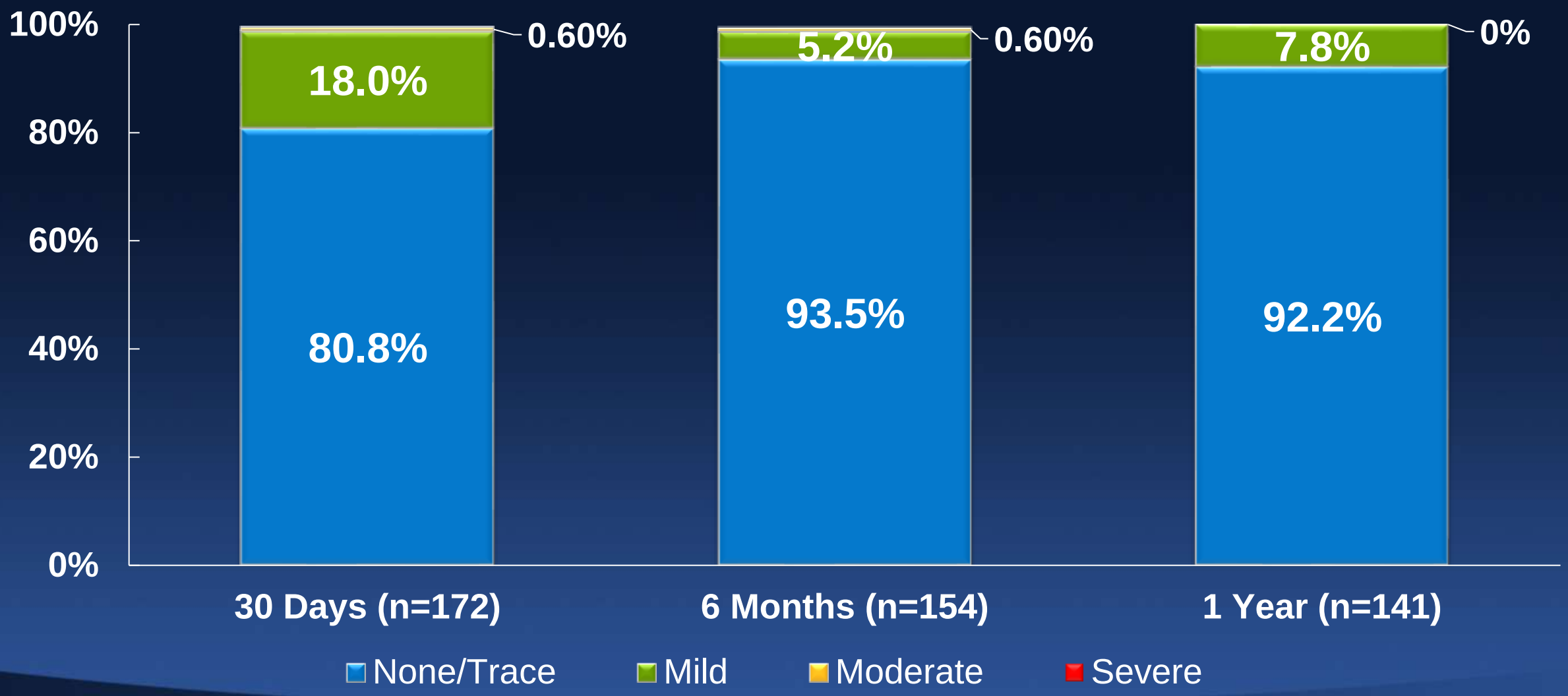


Hemodynamic Valve Performance

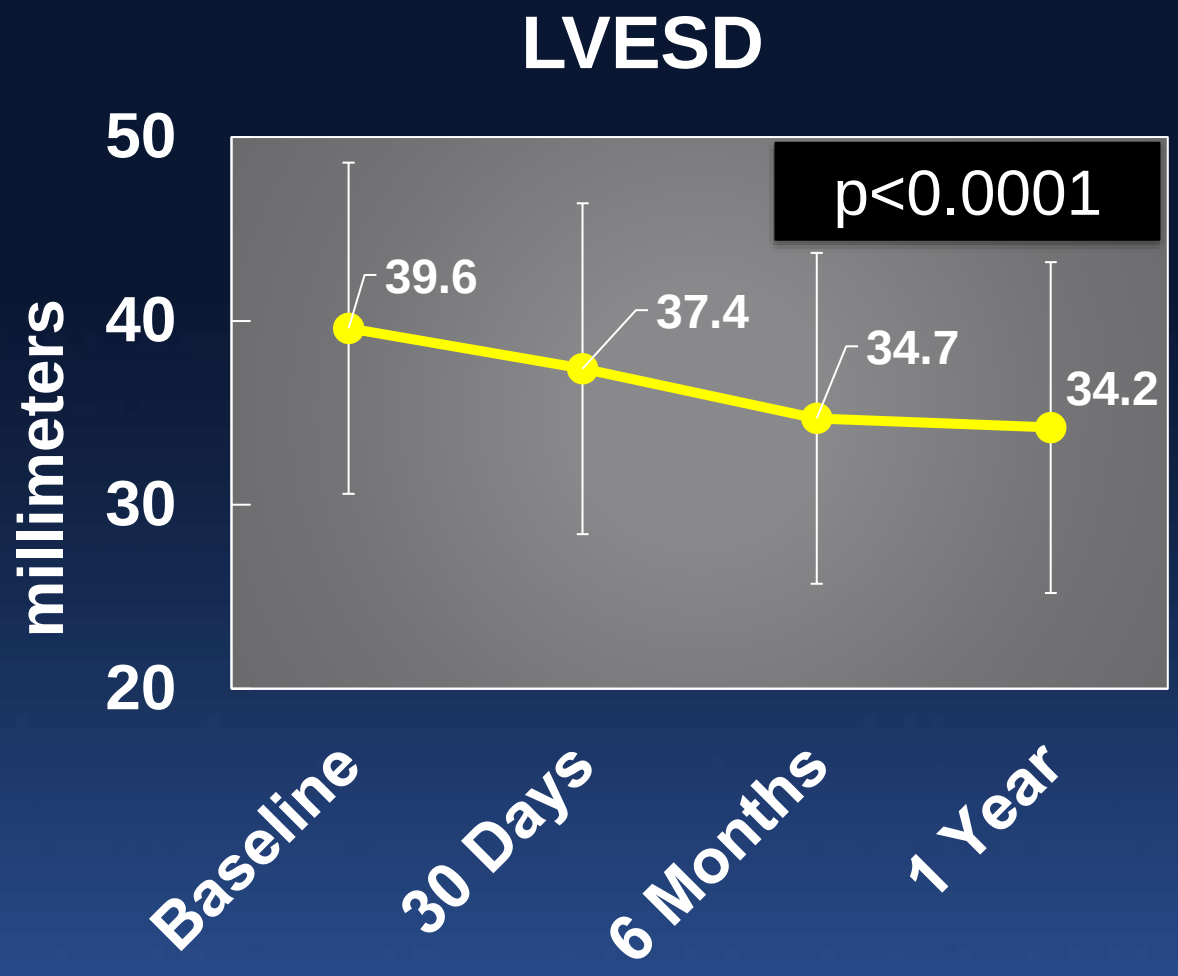


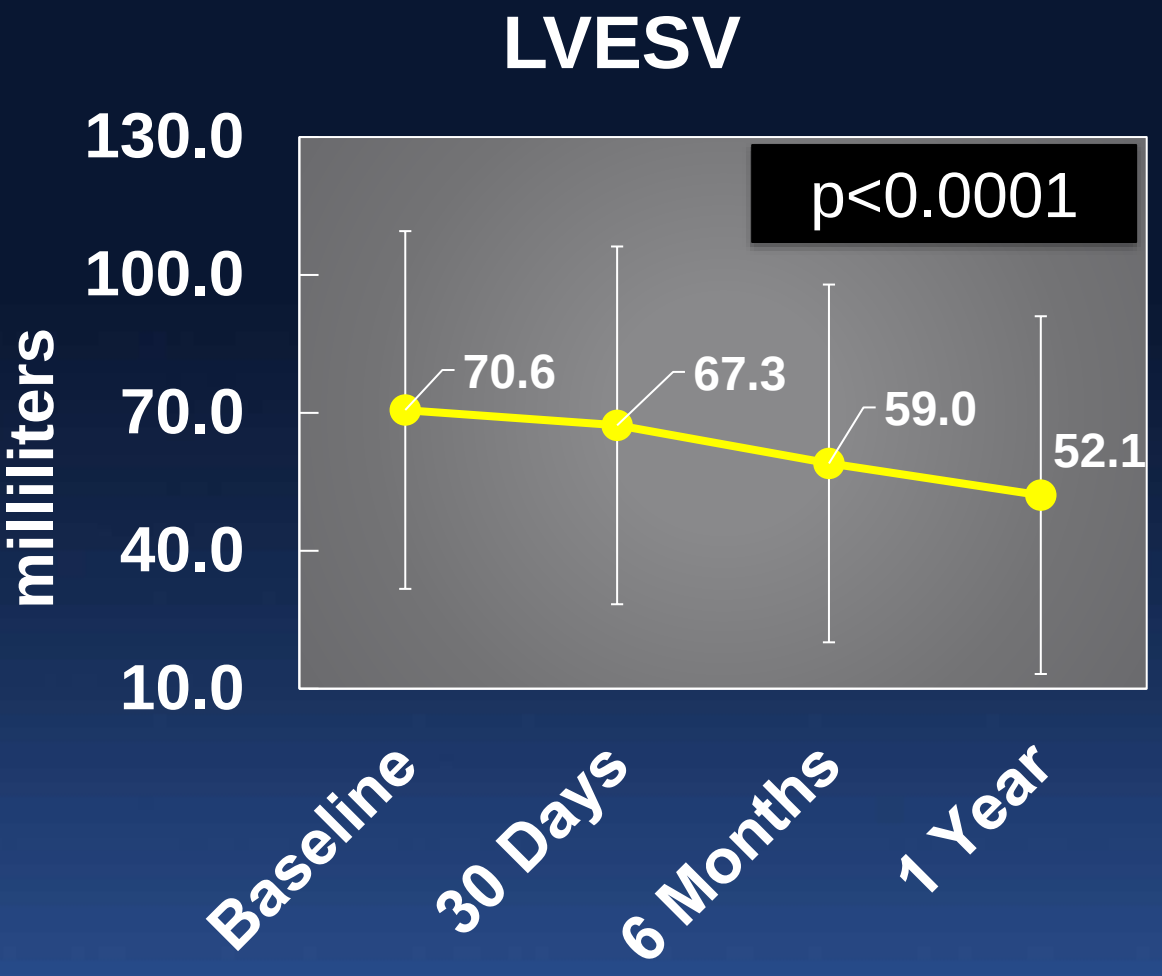
*AVA (cm²)

Paravalvular Regurgitation



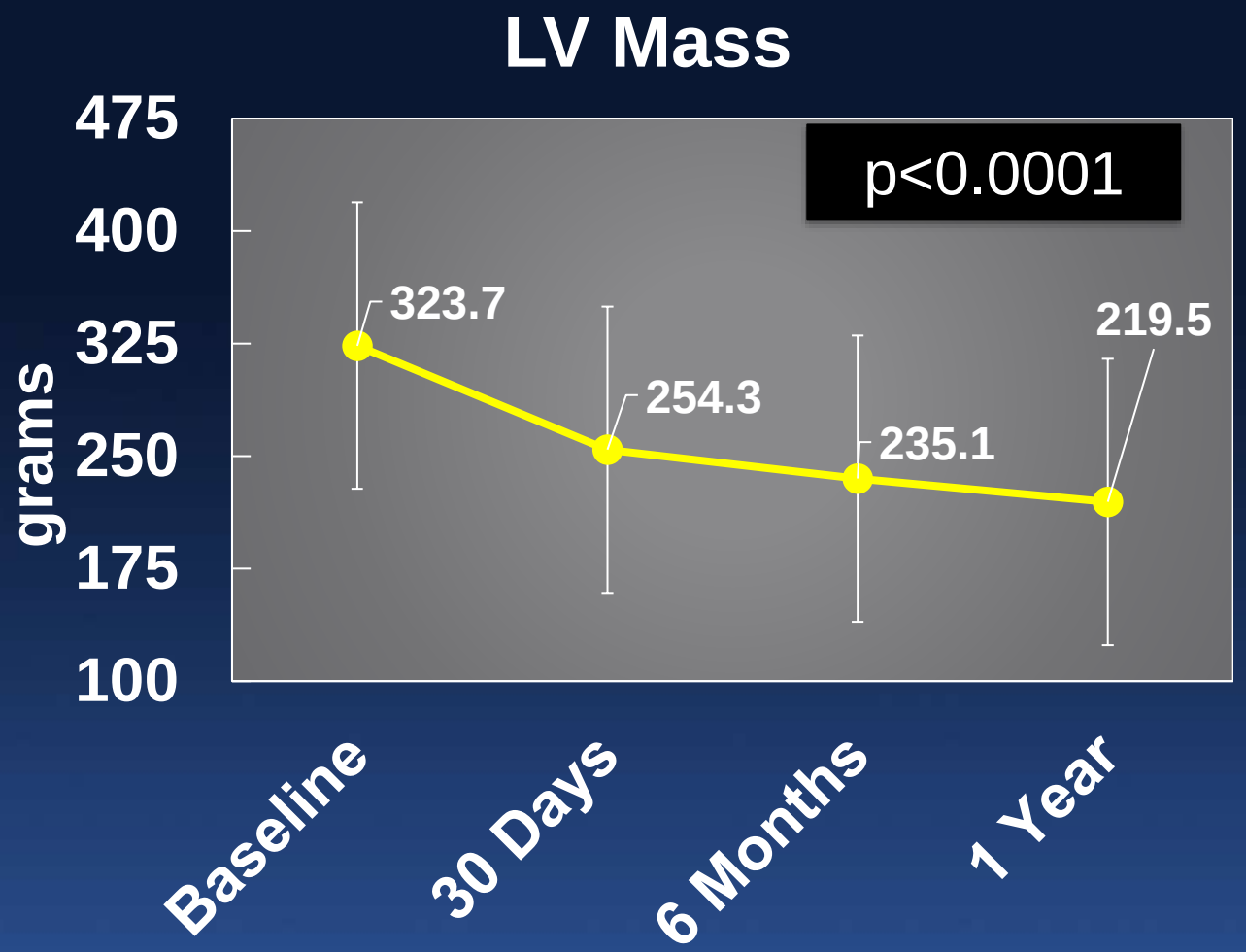
LV Remodeling

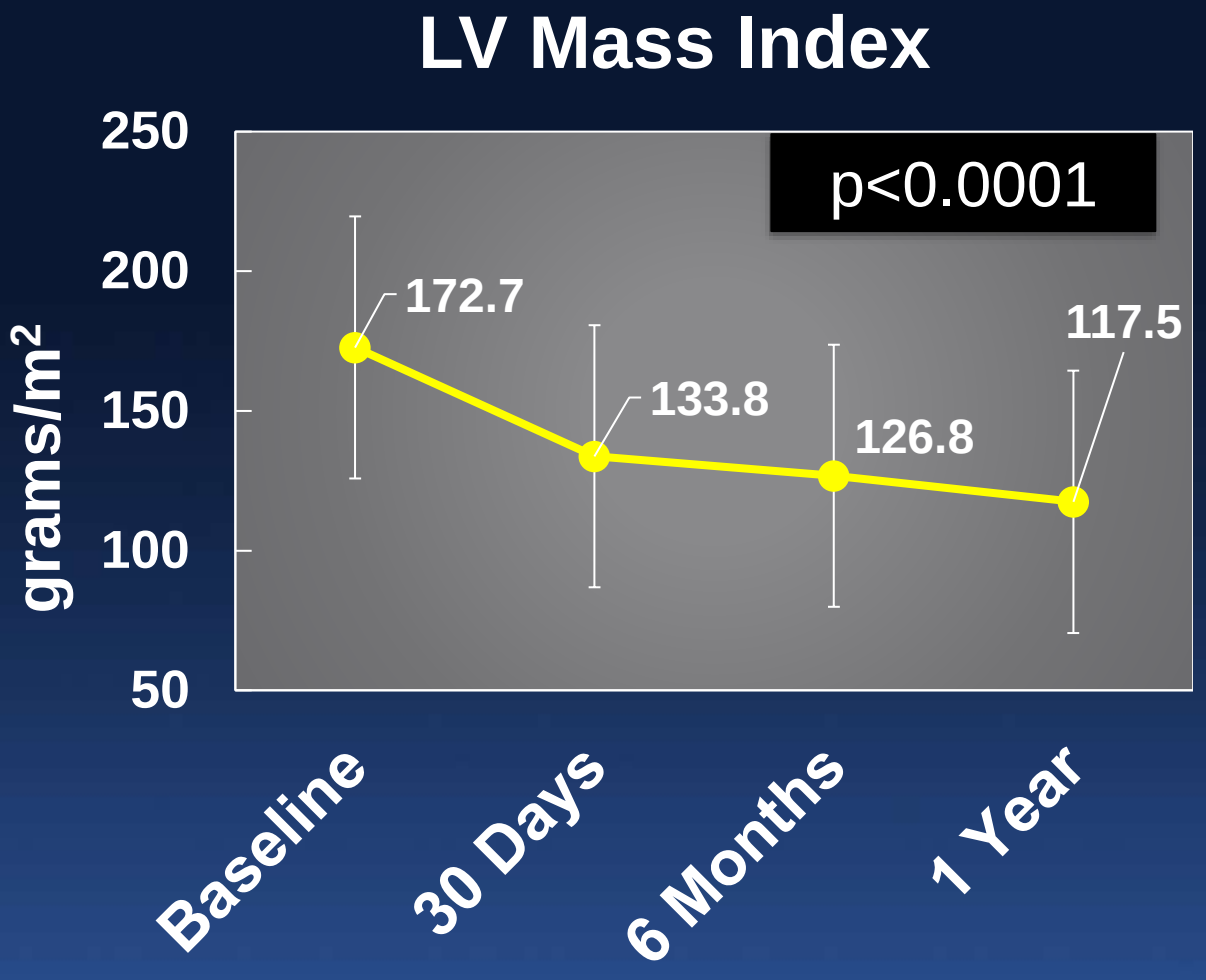




p-value for comparison of baseline to 1 year using paired t-test

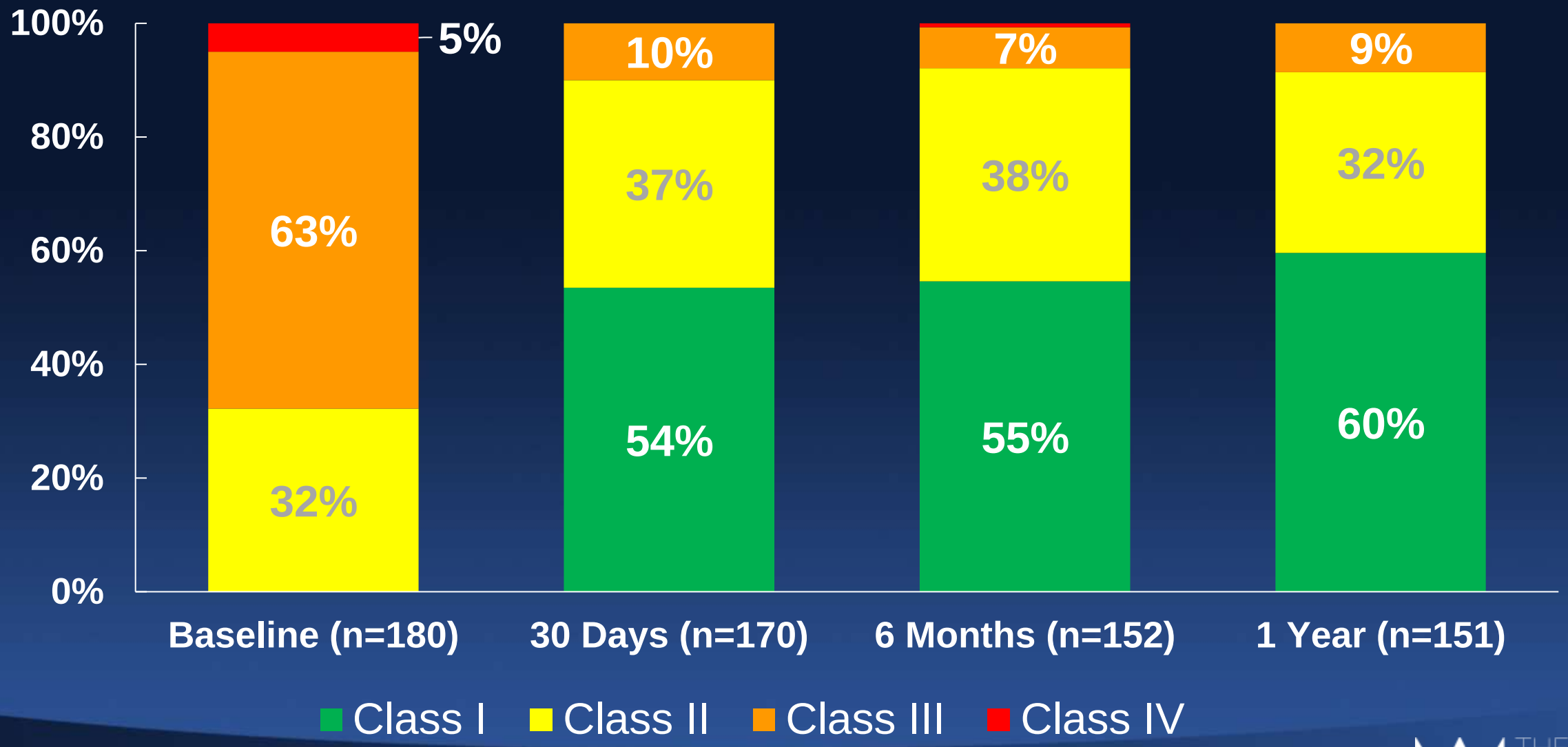
LV Mass



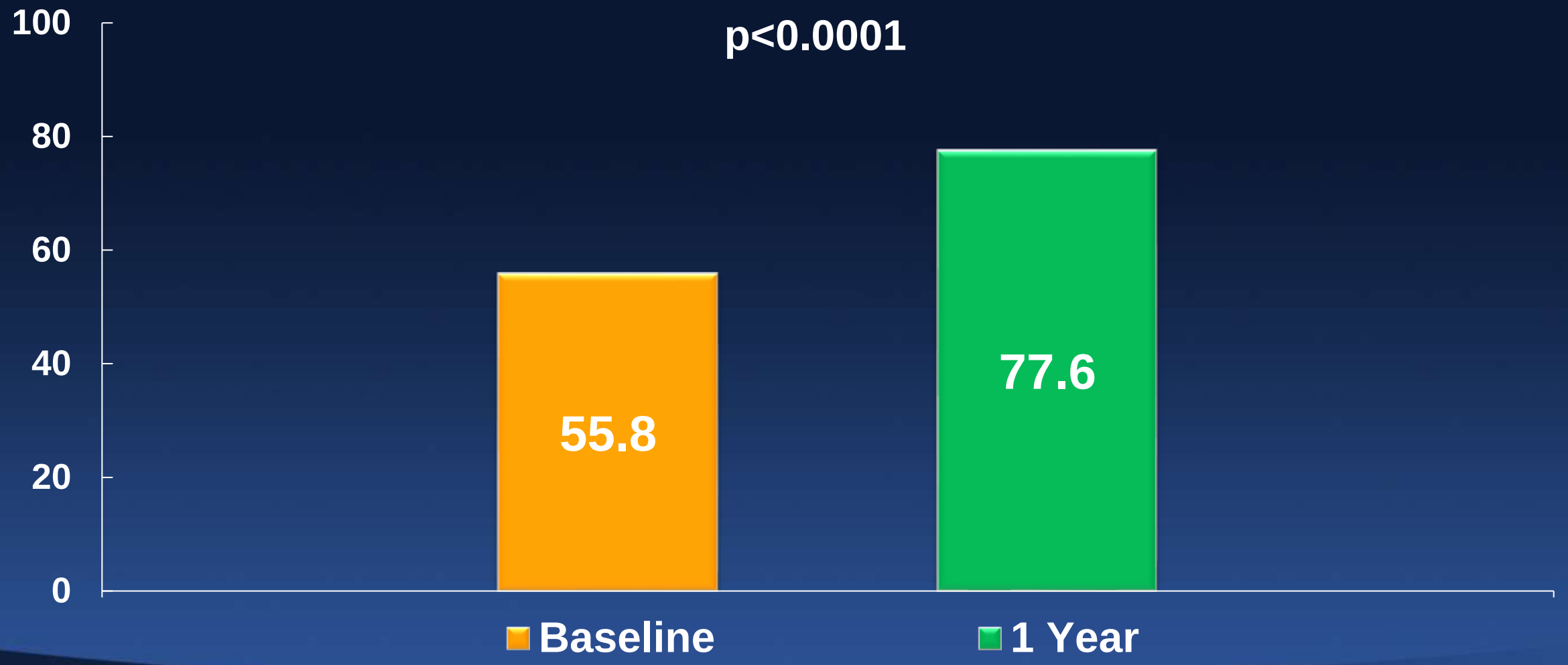


p-value for comparison of baseline to 1 year using paired t-test

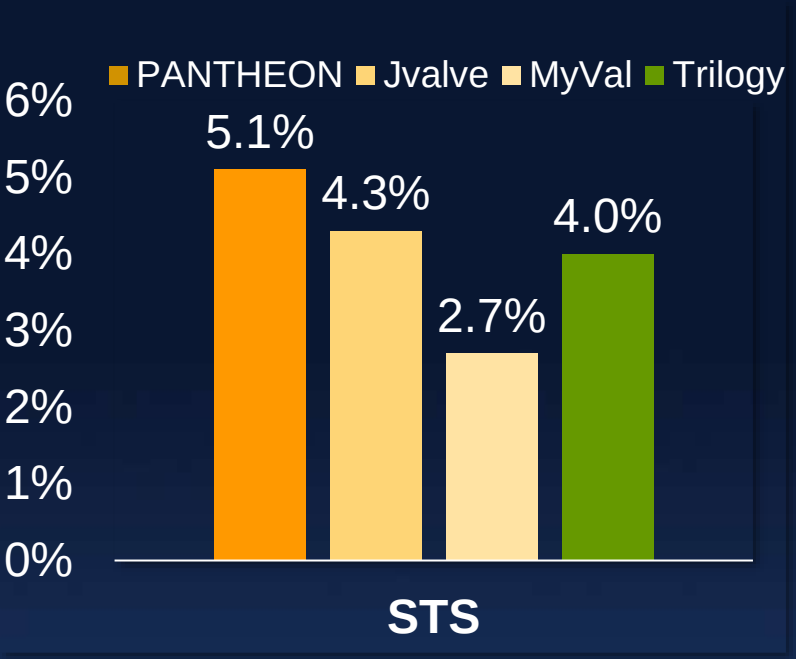
NYHA Functional Class

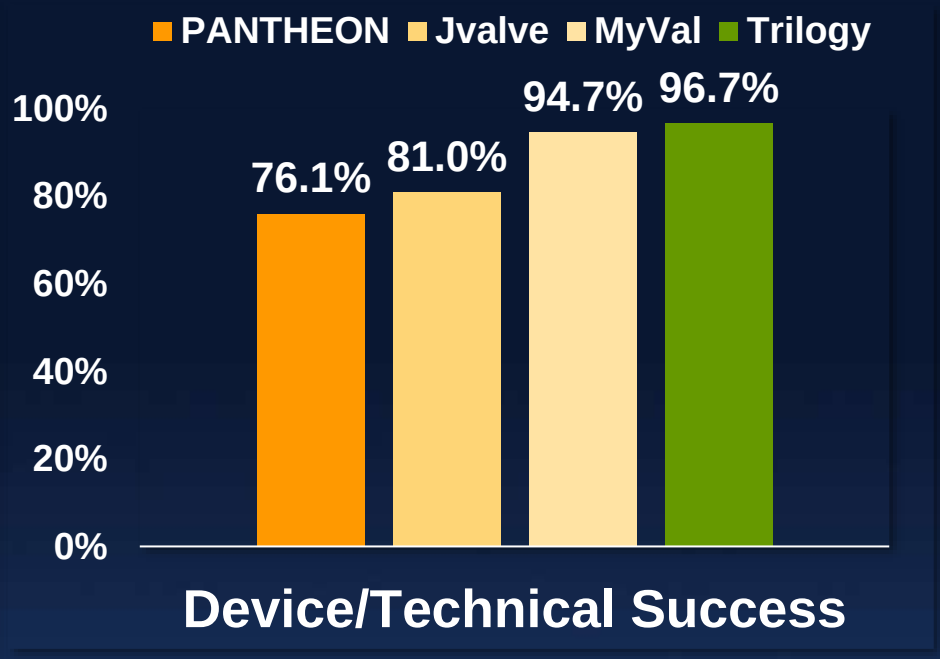


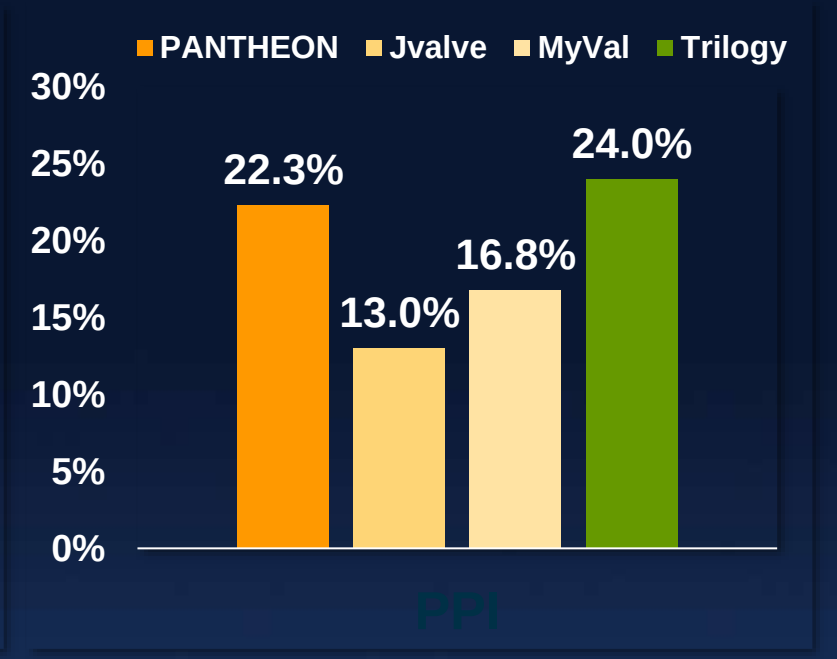
Quality of Life: KCCQ-OS

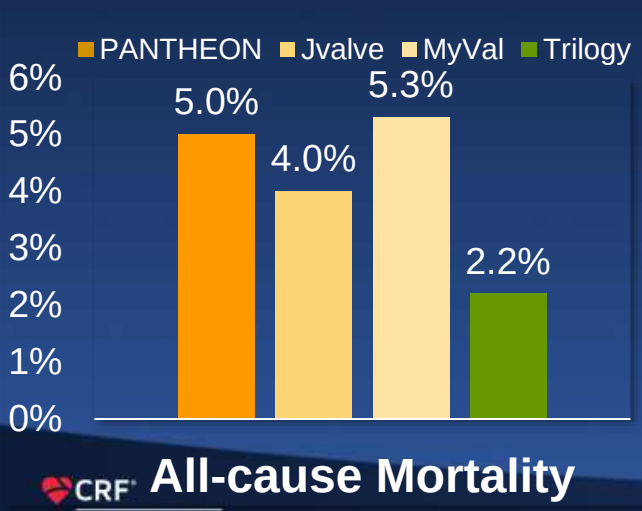


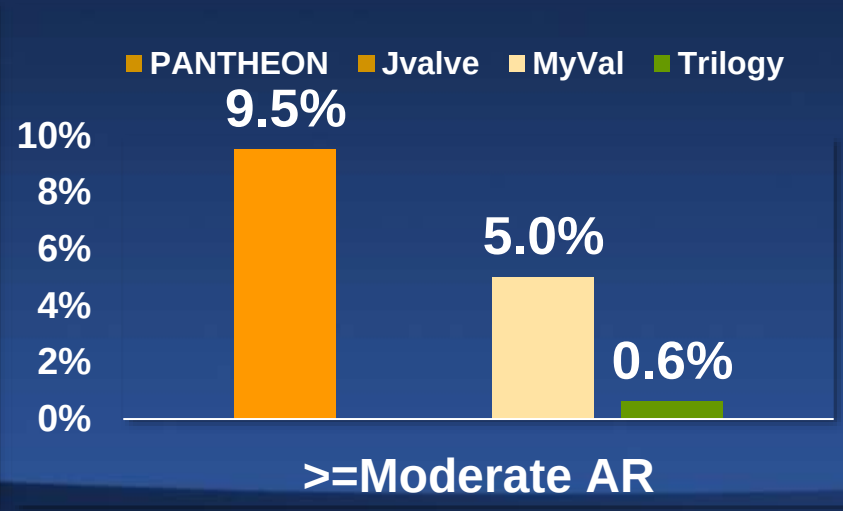
Comparing Studies

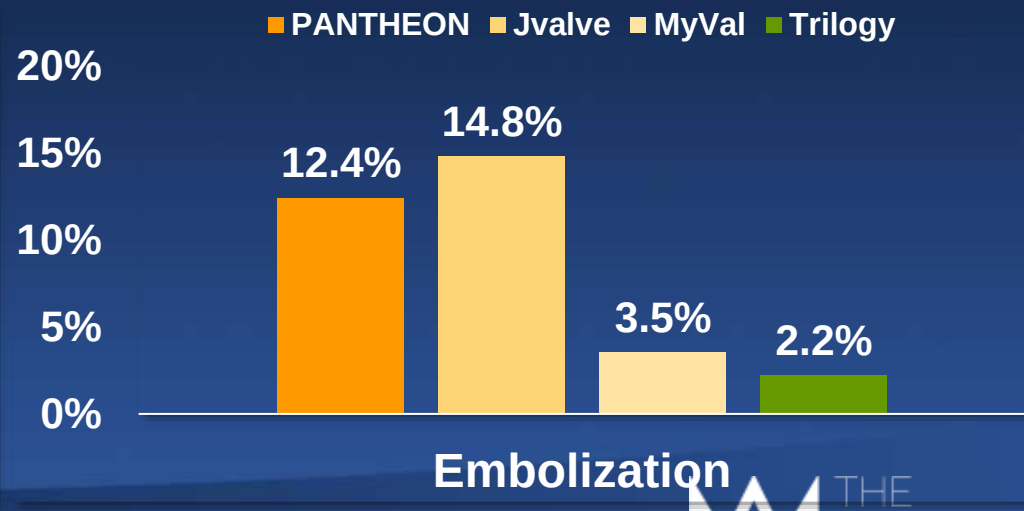












CRF TCT

THE ALIGN AR TRIAL

The ALIGN AR Trial
Conclusions (1)

In a population of symptomatic patients with ≥3+ aortic regurgitation at high surgical risk, TAVR using the Trilogy THV:

- Achieved safety outcomes that met the 30-day performance goal (26.7%, p<0.0001)
- Achieved an efficacy outcome for all-cause mortality that met the 12-month performance goal (7.8%, p<0.0001)
- Among safety endpoints, the rate of new pacemaker implantation was 24.0% and declined during the course of the trial due to changes in implant technique and oversizing strategy

The ALIGN AR Trial
Conclusions (2)

- Trilogy THV performance was excellent with:
  - Large EOA and low transvalvular gradients
  - Low paravalvular regurgitation (0% ≥ Moderate at 1 year)
- Echocardiography demonstrated significant improvement in LV remodeling
- Patients reported sustained improvement in QoL and heart failure functional status through 1 year

The ALIGN AR Trial
Clinical Implications

The TRILOGY THV system provides the first dedicated TAVR option for symptomatic patients with ≥3+ AR who are at high risk for surgery and is well positioned to become the preferred therapy upon approval for this population