Para-valvular Regurgitation after TAVR – The Next "Big Thing"?

Impact on Clinical Outcomes and Treatment

Susheel Kodali, MD

Co-Director, Heart Valve Center

Columbia University

New York, NY

CARDIOVASCULAR RESEARCH FOUNDATION
A Passion for Innovation

COLUMBIA UNIVERSITY MEDICAL CENTER
NewYork-Presbyterian

Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial Interest /arrangement or affiliation with the organization(s) listed below

Affiliation/Financial Relationship	Company
• Consulting Fees/Honoraria	• Edwards Lifesciences, St. Jude Medical, Paieon Medical
• Advisory Board/Equity	• Thubrikar Aortic Valve, Inc

Paravalvular AR and In-Hospital Mortality

German Registry

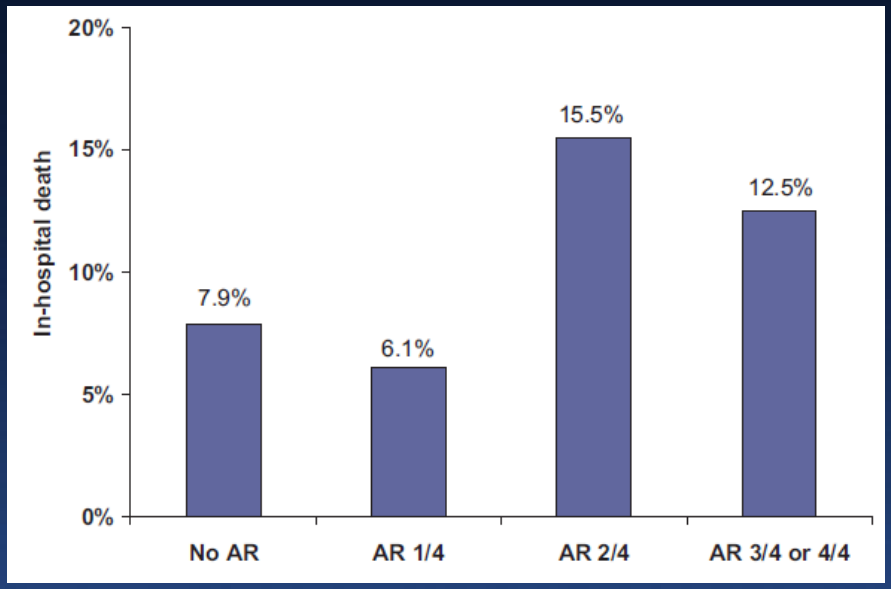


Table 6 Multivariate predictors of the occurrence of at least moderate post-procedural AR (c=0.74)

	OR (95% CI)	p Value
Aortic valve area (per cm^2)	0.10 (0.02 to 0.41)	0.001
Cardiogenic shock	1.94 (1.18 to 3.21)	0.009
Annulus estimation by TOE	1.94 (1.14 to 3.29)	0.01
Renal failure	0.53 (0.33 to 0.85)	0.01
Male gender	1.80 (1.07 to 3.06)	0.02
Bicuspid aortic valve	2.95 (0.73 to 11.89)	0.12
Corevalve prosthesis	1.58 (0.73 to 3.40)	0.25

AR, aortic regurgitation; TOE, transoesophageal echocardiography.

Abdel-Wahab et al. Heart, 97:889; 2011

Paravalvular AR and Long Term Mortality

Italian Registry

Incidence and Predictors of Early and Late Mortality After Transcatheter Aortic Valve Implantation in 663 Patients With Severe Aortic Stenosis

Corrado Tamburino, MD, PhD; Davide
Anna Sonia Petronio, MD; Federica Ettori, M
Francesco Bedogni, MD; Francesco Maisano,
David Antoniucci, MD; Massimo Nap
Claudia Fiorina, MD

Table 4. Multivariate Analysis

	Hazard Ratio	95% LCL	95% UCL	*P* Value
Overall mortality				
Intraprocedural stroke	15.76	3.27	75.90	0.001
Pre-procedural mitral regurgitation 3+ or 4+	4.62	1.66	12.87	0.003
Systolic pulmonary artery pressure >60 mm Hg	3.21	1.19	8.71	0.02
Prior acute pulmonary edema	2.75	1.32	5.72	0.007
Diabetes mellitus	2.45	1.19	5.07	0.02
Late mortality				
Prior stroke	5.468	1.47	20.39	0.01
Post-procedural paravalvular leak ≥2+	3.785	1.57	9.10	0.003
Prior acute pulmonary edema	2.696	1.09	6.68	0.03
Chronic kidney disease	2.532	1.01	6.35	0.048

LCL indicates lower confidence limit; UCL indicates upper confidence limit.

Postprocedural paravalvular leak ≥ 2 (HR 3.79), was an independent predictors of mortality between 30 days and 1 year.

Tamburino C et al. Circ 2011:123 (3): 299-308.

Paravalvular AR and Long Term Mortality

UK Registry

Long-Term Outcomes After Transcatheter Aortic Valve Implantation in High-Risk Patients With Severe Aortic Stenosis

The U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantat

Neil E. Moat, MBBS, MS,* Peter Ludman, MA
Ben Bridgewater, PHD,§ Andrew D. Cunningh
Martyn Thomas, MD,¶ Jan Kovac, MD,# Tom
Olaf Wendler, MD, PHD,** David Hildick-Smi
Uday Trivedi, MBBS,†† Daniel J. Blackman, M
Stephen J. D. Brecker, MD,§§ Andreas Baumb
Huon Gray, MD,## Michael J. Mullen, MBBS

JACC Vol. 58, No. 20, 2011
November 8, 2011:2130–8

Table 3 Predictors of Mortality at 1 Year

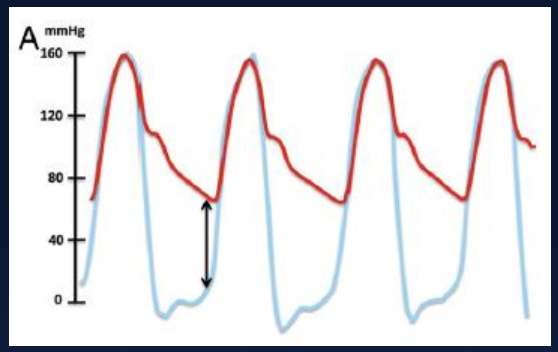
Variables	Alive (n = 684)	Dead (n = 186)	Univariate Model	p Value	Multivariate Model	p Value
Edwards SAPIEN	321/680 (47.2)	89/182 (48.9)	1.00			
Medtronic CoreValve	359/680 (52.8)	93/182 (51.1)	0.95 (0.70–1.29)	0.75		
Route, other	196/684 (28.7)	75/186 (40.3)	1.00			
Route, transfemoral	488/684 (71.3)	111/186 (59.7)	0.65 (0.48–0.88)	0.006	0.73 (0.52–1.04)	0.08
AR moderate/severe	83/674 (12.3)	32/175 (18.3)	1.49 (1.00–2.21)	0.048	1.66 (1.10–2.51)	0.016
Major vascular complication	39/684 (5.7)	16/185 (8.7)	1.42 (0.82–2.45)	0.21		
Permanent pacemaker	108/683 (15.8)	33/184 (17.9)	1.21(0.83–1.77)	0.32		
Male	355/684 (59.9)	101/186 (54.3)	1.19 (0.88–1.61)	0.25		
Age, yrs	81.8 ± 7.3	82.3 ± 6.4	1.01 (0.99–1.03)	0.52		
LVEF <30%	52/680 (7.6)	22/185 (11.9)	1.89 (1.16–3.07)	0.01	1.65 (0.98–2.79)	0.06
NYHA functional class I/II	160/680 (23.5)	39/186 (21.0)	1.00			
NYHA functional class III/IV	520/680 (76.5)	147/186 (79.0)	1.14 (0.79–1.63)	0.50		
Coronary disease	301/653 (46.1)	93/175 (53.1)	1.38 (1.01–1.87)	0.04	1.23 (0.88–1.73)	0.23
Any previous cardiac surgery	202/667 (30.3)	57/186 (30.7)	1.04 (0.75–1.43)	0.83		
PVD	179/654 (27.4)	62/178 (34.8)	1.28 (0.91–1.75)	0.16		
Diabetes mellitus	146/675 (21.6)	50/136 (26.9)	1.36 (0.98–1.89)	0.07		
COPD	176/654 (26.9)	63/180 (35.0)	1.40 (1.02–1.93)	0.04	1.41 (1.00–1.98)	0.05
Creatinine >200 mmol/l	38/668 (5.7)	19/185 (10.3)	1.84 (1.14–2.97)	0.012	1.55 (0.90–2.68)	0.11

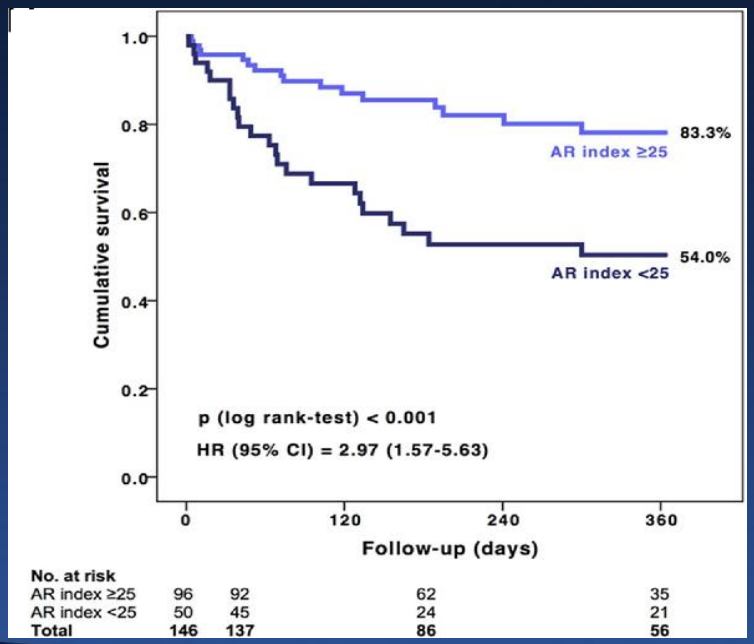
AR moderate/severe 83/674 (12.3) 32/175 (18.3) 1.49 (1.00–2.21) 0.048 1.66 (1.10–2.51)

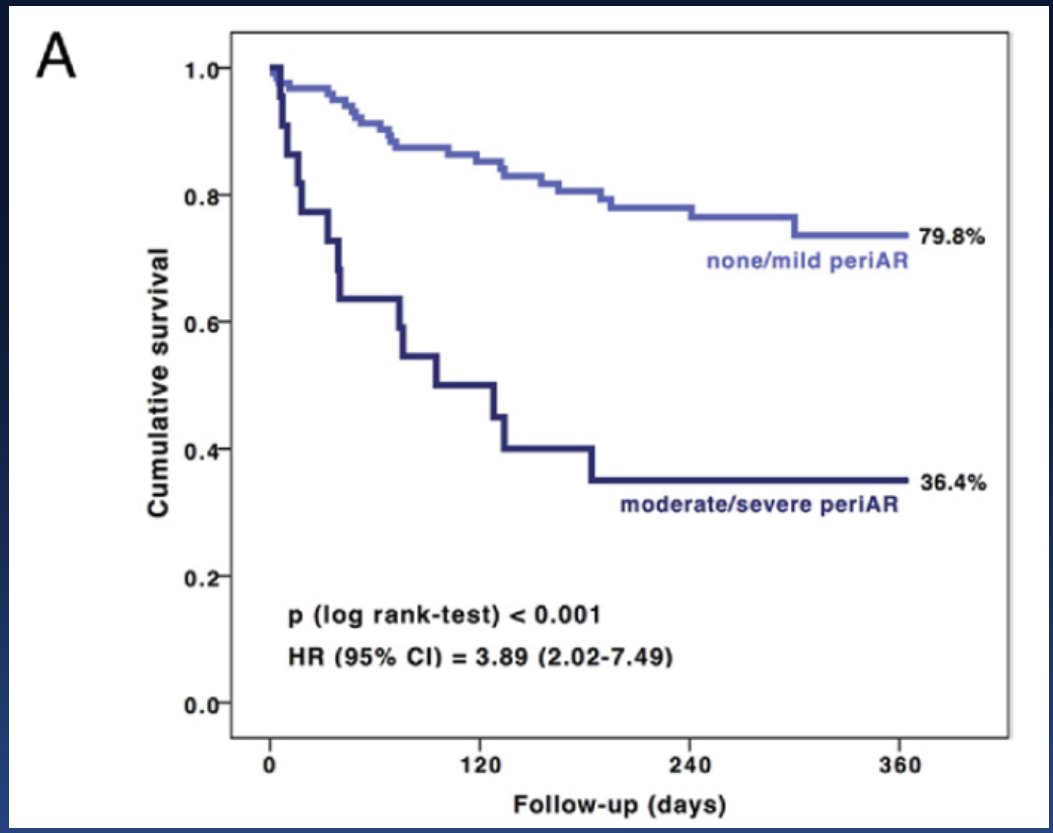
Values are n/N (%), mean ± SD, or hazard ratio (95% confidence interval).
CI = confidence interval; HR = hazard ratio; other abbreviations as in Tables 1 and 2.

J Am Coll Cardiol 2011;58:2130–8)

Clinical Impact of Severity of Paravalvular Regurgitation Corroborated by Invasive Index







AR Index = (DBP-LVEDP)/SBP

Sinning et al. JACC, 59:1134-41; 2012

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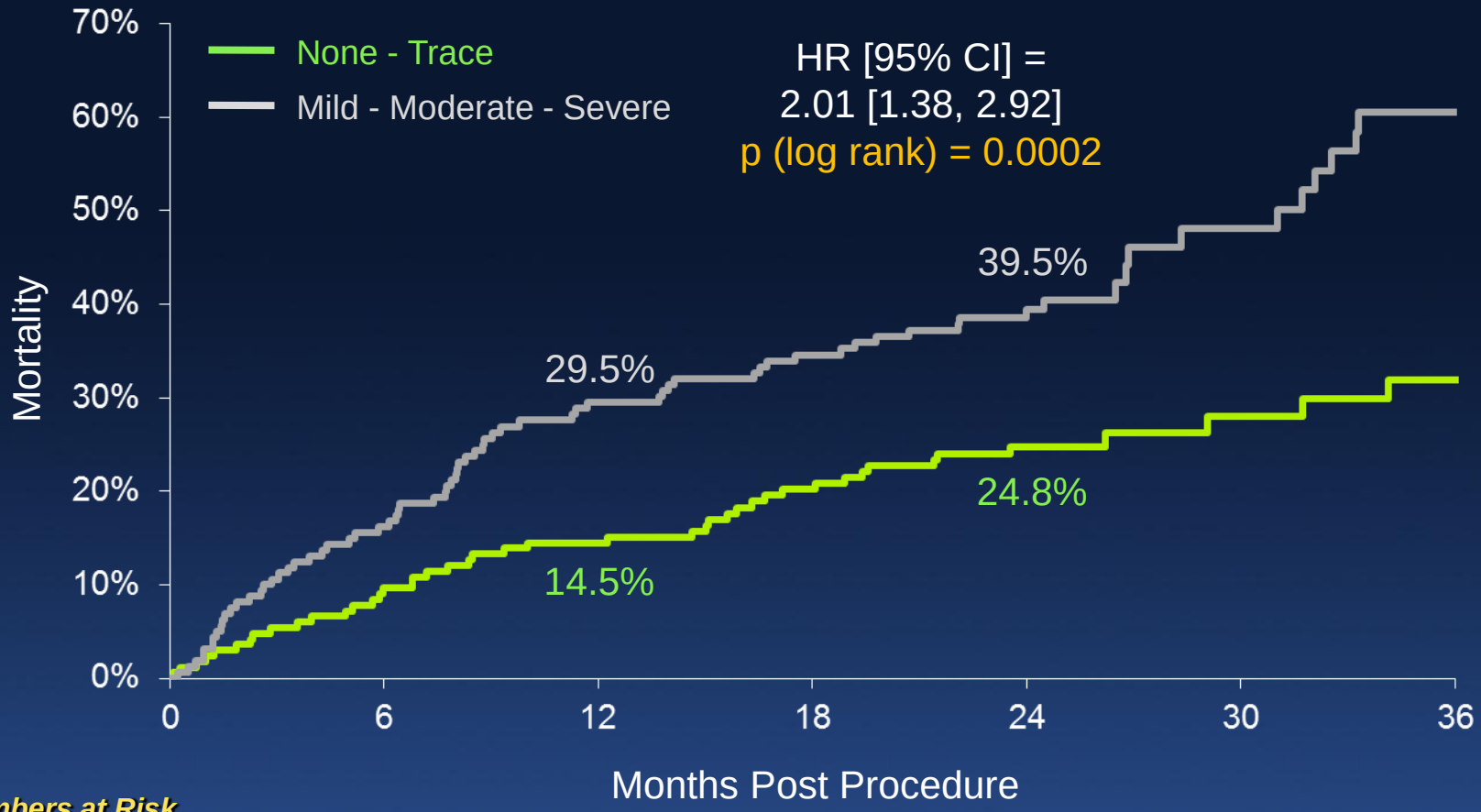
Paravalvular AR and Mortality

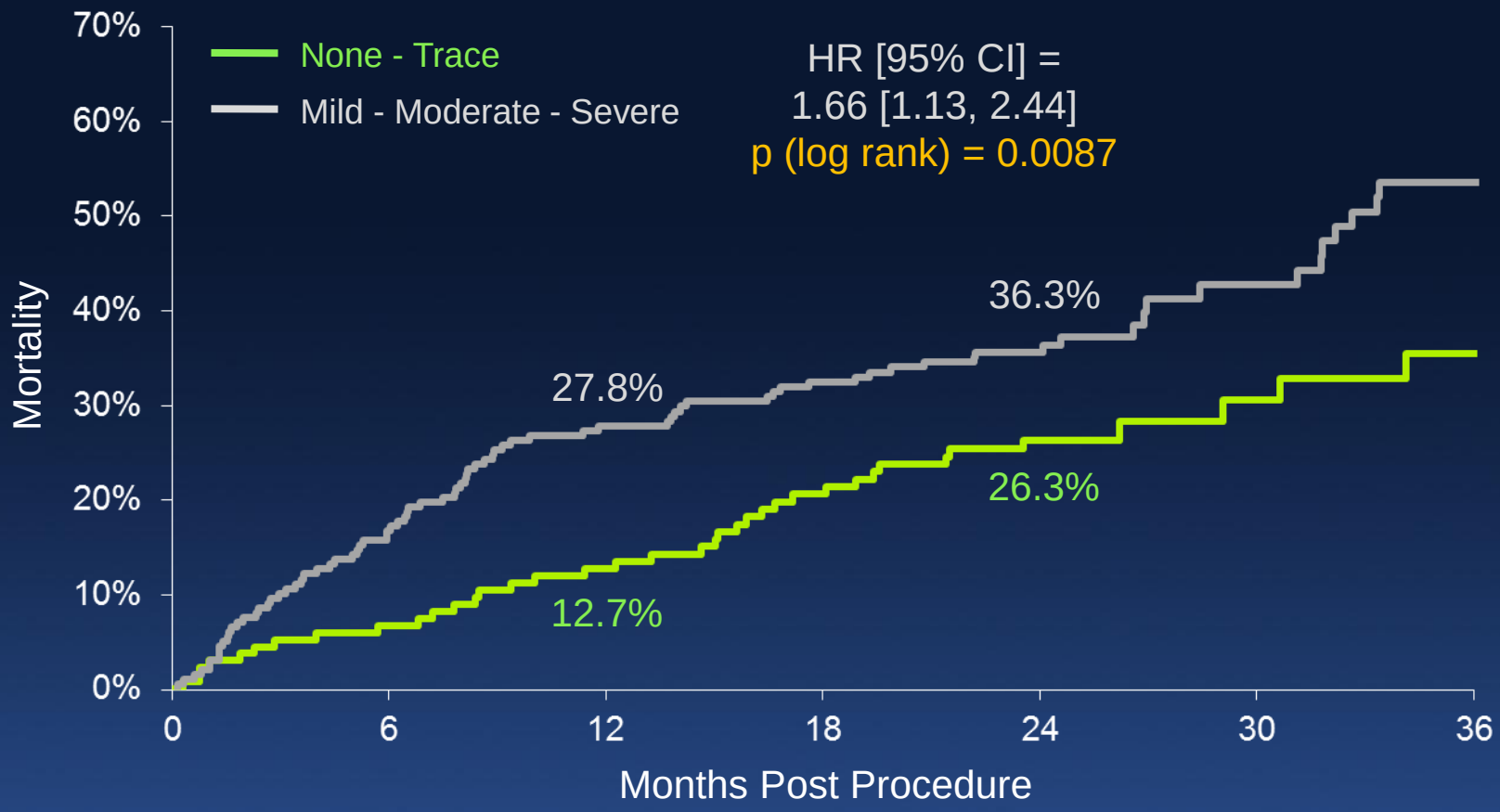
PARTNER Trial – Cohort A



Numbers at Risk

None-Tr	167	149	140	126	87	41	16
Mild-Mod-Sev	160	134	112	101	64	26	12

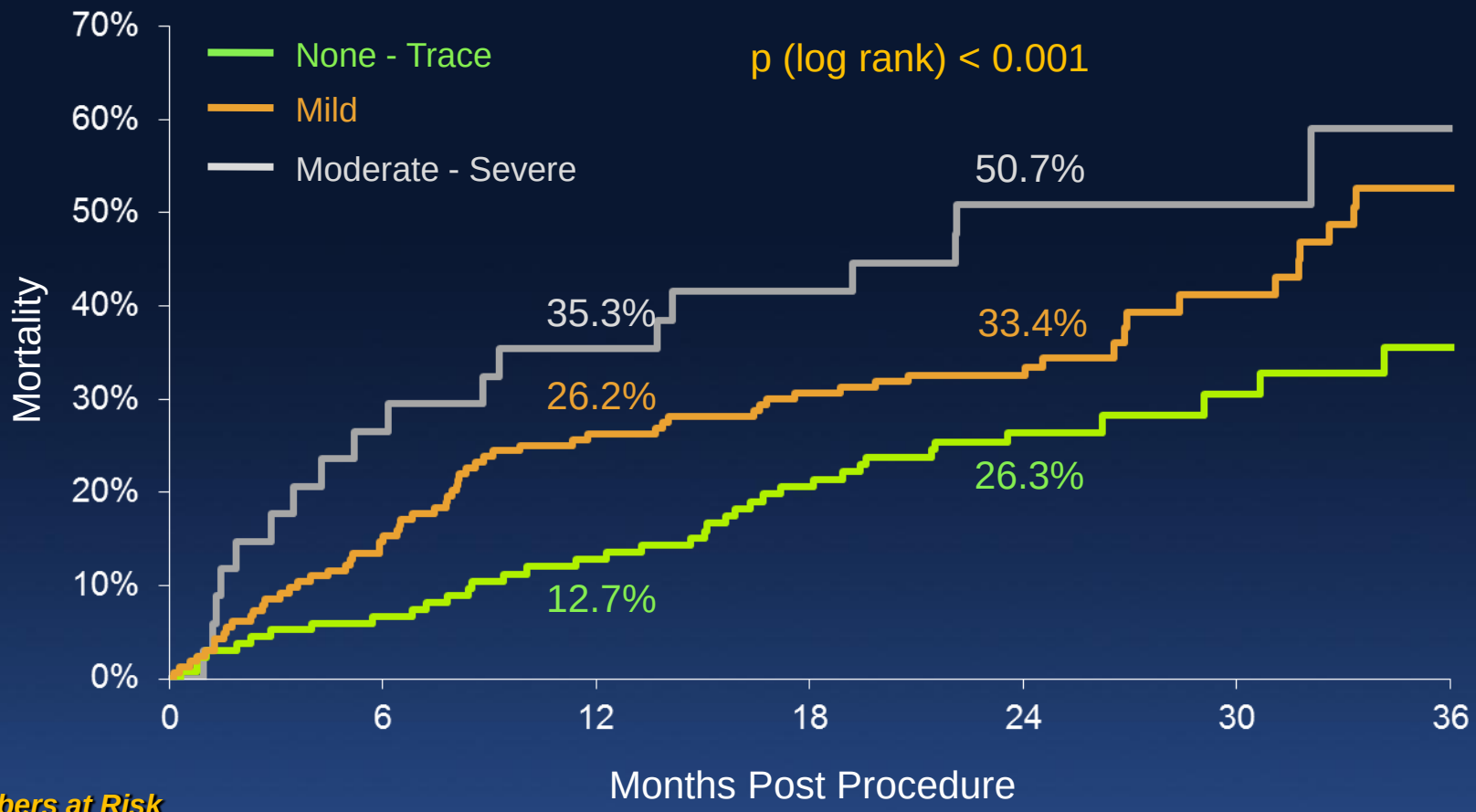
Total AR and Mortality
PARTNER Trial – Cohort A



Numbers at Risk

None-Tr	135	125	115	101	68	31	11
Mild-Mod-Sev	199	164	143	130	86	39	18

Total AR and Mortality
PARTNER Trial – Cohort A



Numbers at Risk

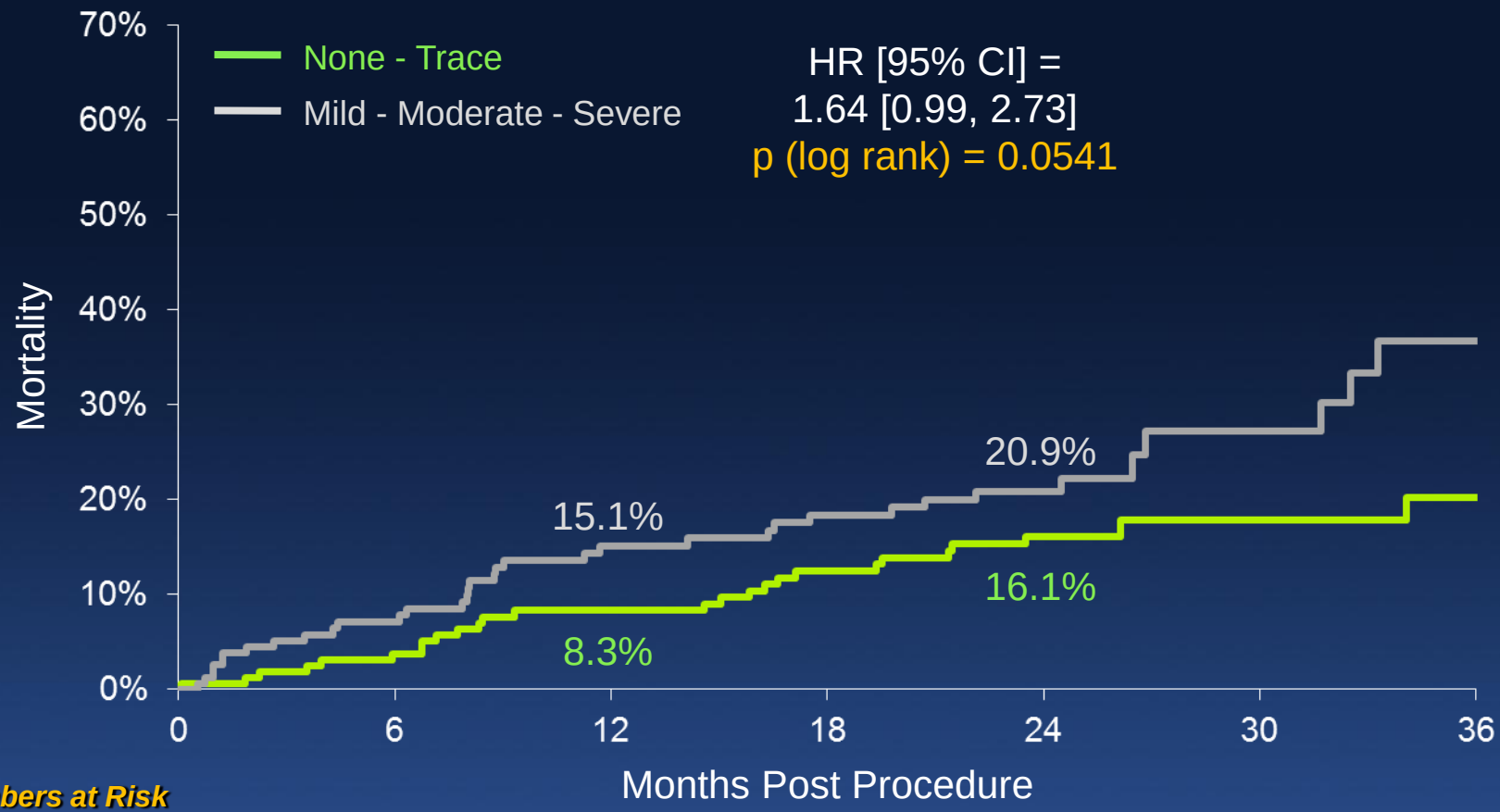
None-Tr	135	125	115	101	68	31	11
Mild	165	139	121	111	71	33	16
Mod-Sev	34	25	22	19	15	6	2

Baseline Echo Characteristics

Stratified by PVL

Characteristic	*None-Trace PVL*	*Mild-Severe PVL*	*p-value*
Baseline AVA (cm^2)	0.65	0.67	0.31
Baseline LV Mass (gm)	268.4 ± 84.7	299.5 ± 81.4	<0.02
Baseline LV Diastolic Volume (cc)	114.8 ± 46.3	132.1 ± 49.4	0.07
Baseline LV Ejection Fraction (%)	51.1	54.0	0.06

PVL Severity and Cardiovascular Mortality
TAVR Patients (AT)



Numbers at Risk

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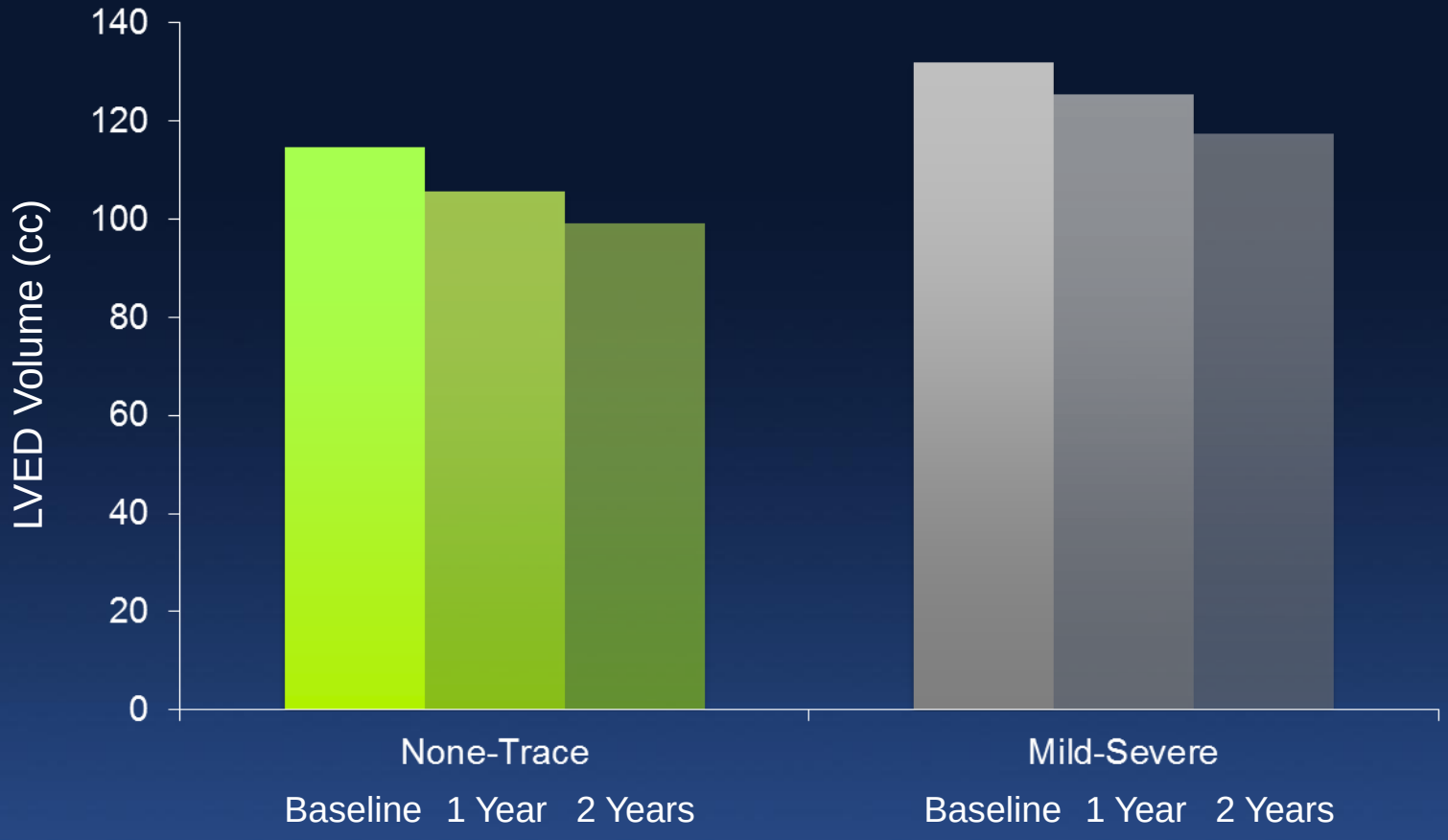
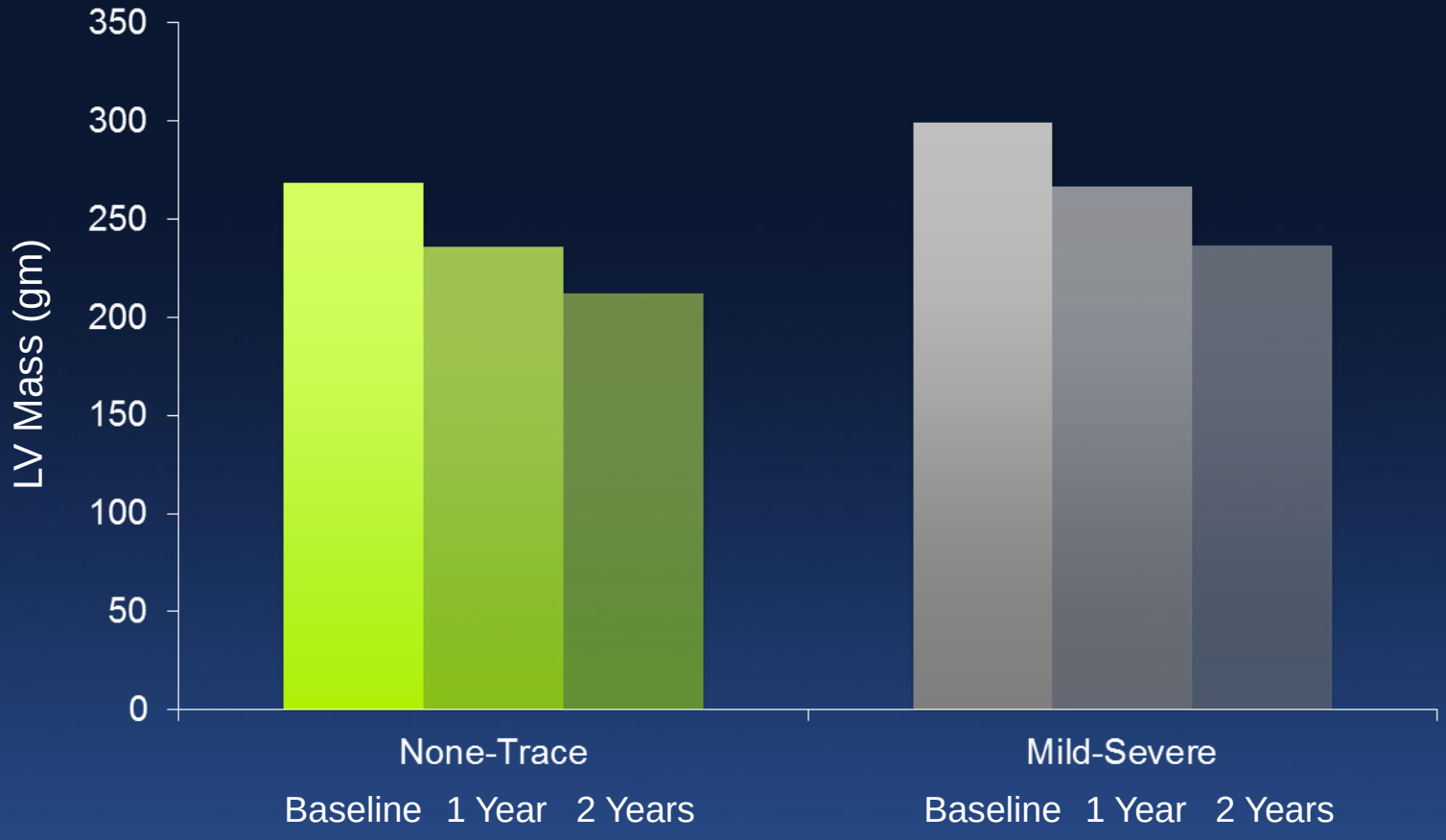
LVED Volume Changes Stratified by Post-Procedure PVL



LV Mass Changes Stratified by Post-Procedure PVL



Treatment of AR Depends on the Etiology

- Native Aortic valve morphology
  - Number of cusps
  - Symmetry/severity of calcification
- Undersizing of the THV
  - Annular measurement
- Malpositioning of the THV
  - Aortic root morphology
  - Mitral valve calcification
  - Sigmoid septum

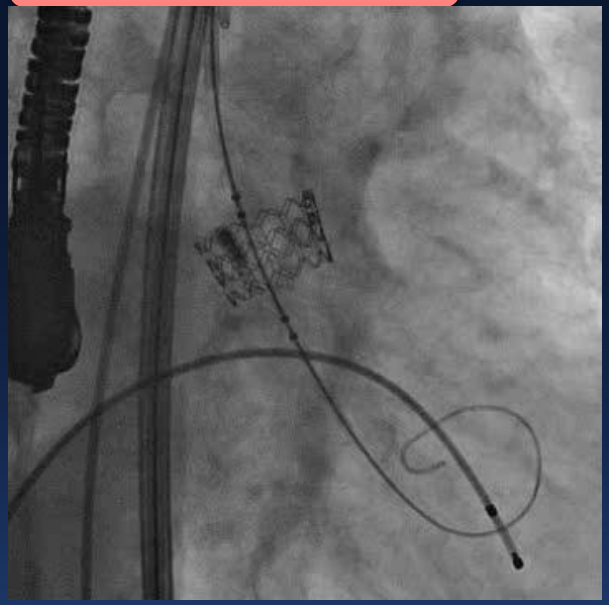
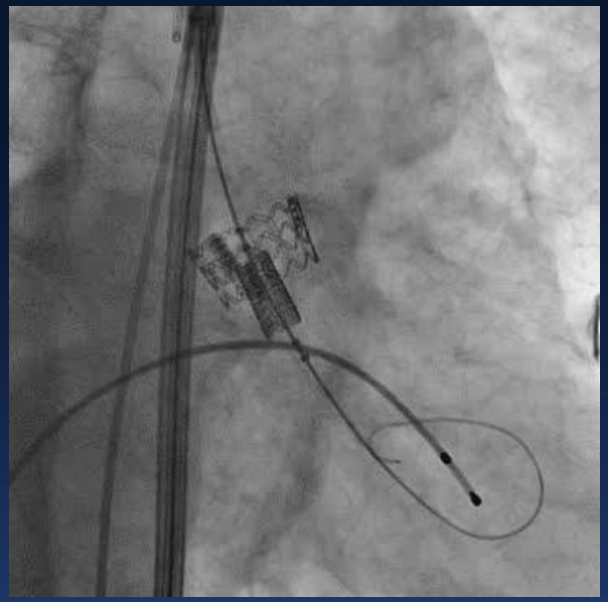
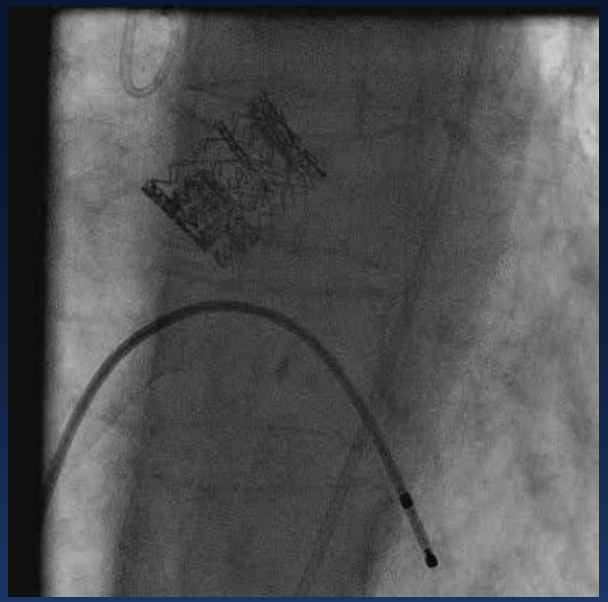
Circularity of THV

THV “seal”

Position of THV influenced by “AV complex”

Significant Paravalvular Aortic Regurgitation
Valve Malposition

Valve too high

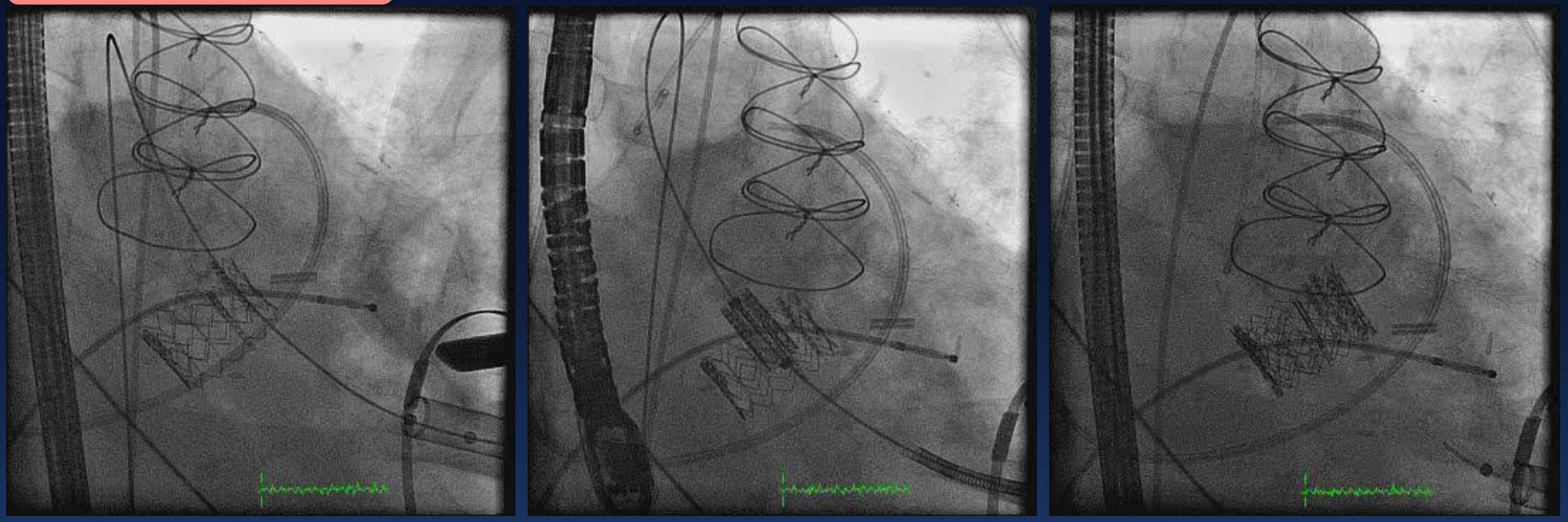
- **THV not stable in the aortic annulus**

Management

- **Pressors to stabilize hemodynamics**
- **CPB likely not useful**
- **Valve-in-valve procedure should be performed immediately**

Significant Paravalvular Aortic Regurgitation
Valve Malposition

Valve too low



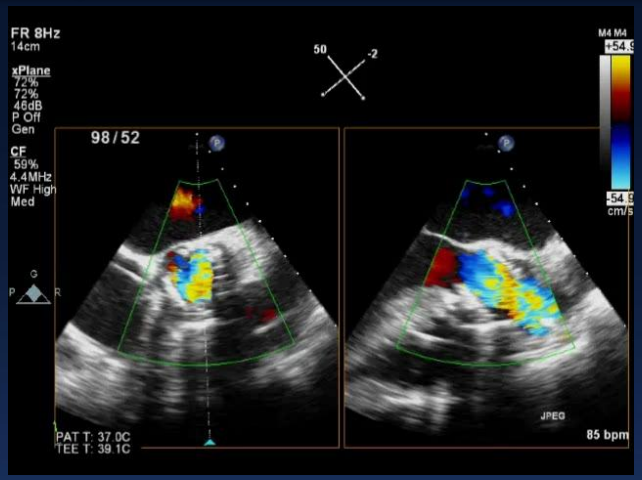
If significant paravalvular jets (flow through struts) are created due to valve malpositioning, consider implanting a second THV

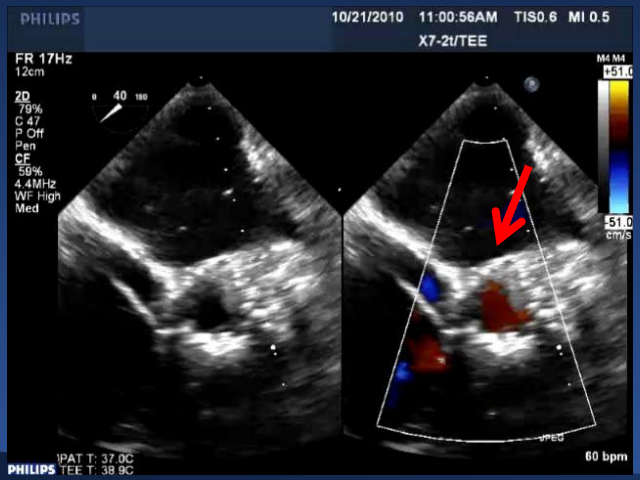
Management

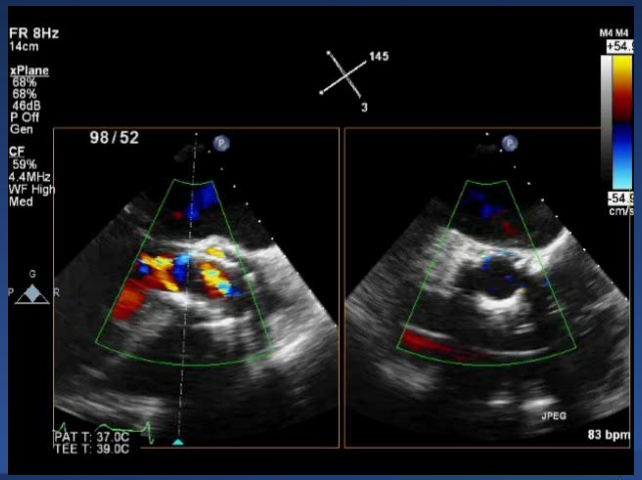
- **Pressors to stabilize hemodynamics**
- **CPB likely not useful**
- **Valve-in-valve procedure should be performed immediately**

Post-Implantation:
Assess THV Function

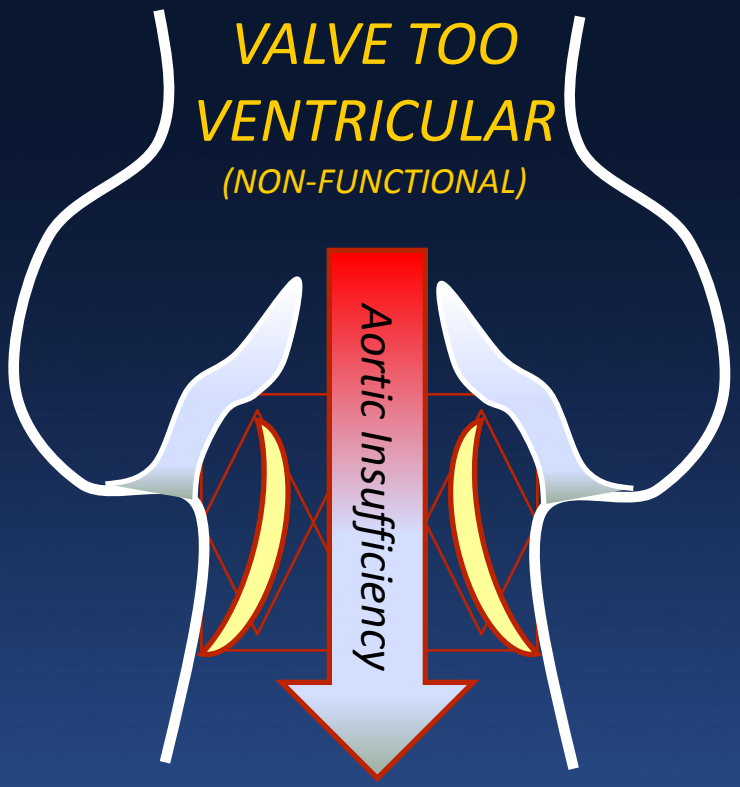
Severe central aortic regurgitation should raise the possibility of primary THV failure







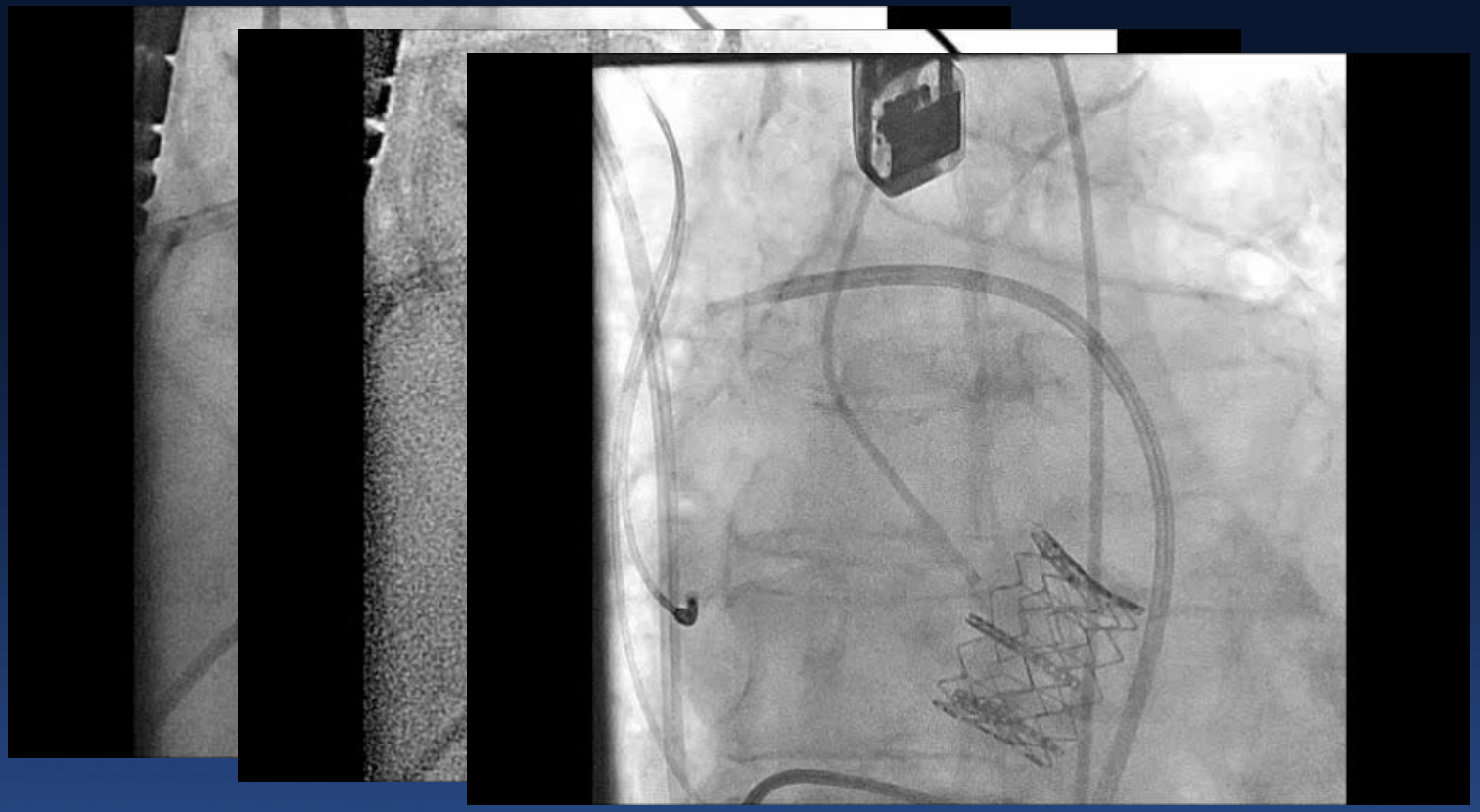
Significant Central Aortic Regurgitation



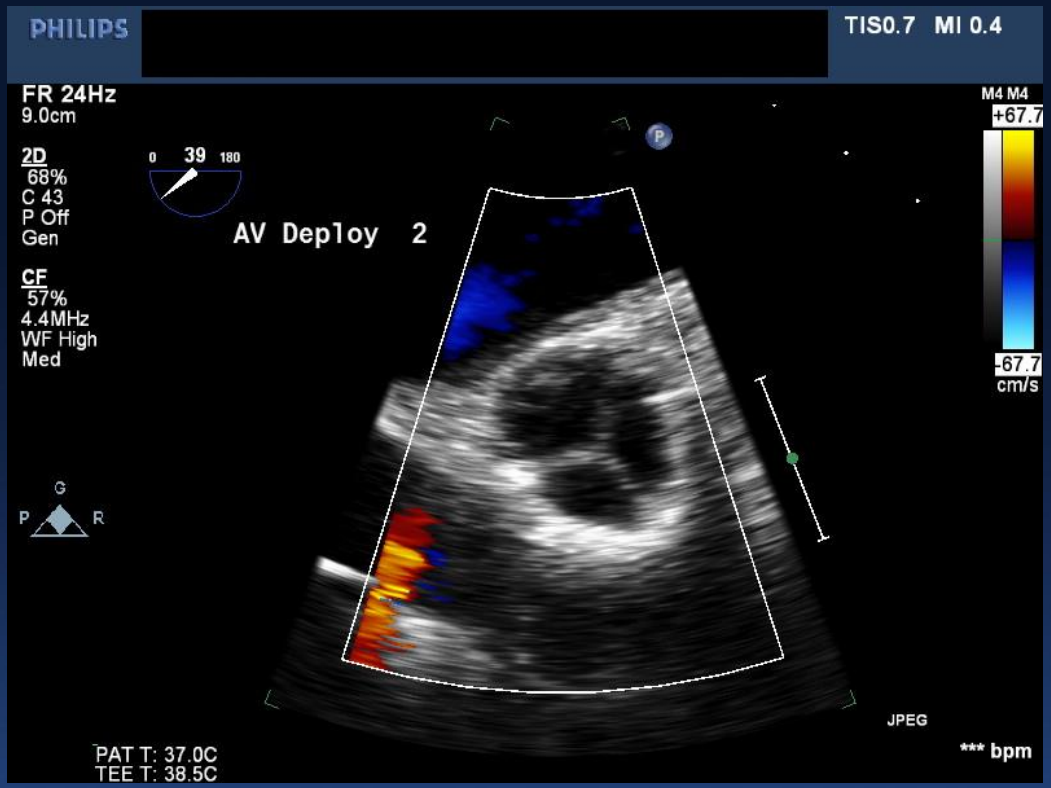
Management

- Evaluate echo closely to determine etiology – frozen leaflet vs leaflet overhang
- Mechanical manipulation of the leaflet with a diagnostic catheter, if frozen leaflet
- Prepare another valve (valve-in-valve procedure) simultaneously
- Mechanical support not very useful with severe AR
- Convert to open-heart surgery?

Significant Central Aortic Regurgitation THV Leaflet Manipulation with Catheter



Significant Central Aortic Regurgitation Valve in Valve



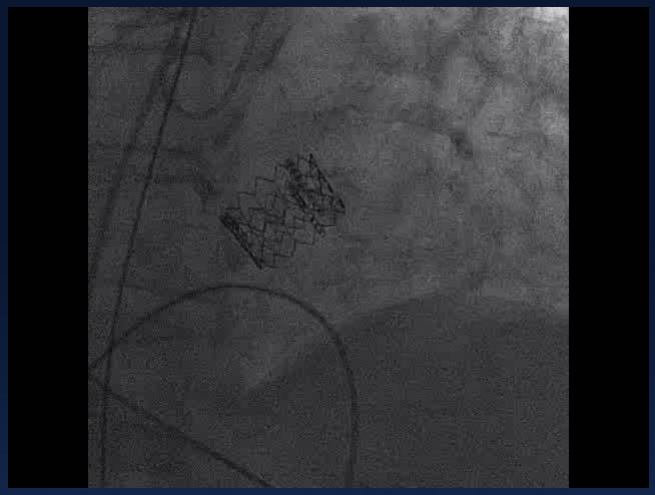
Significant Paravalvular Aortic Regurgitation Size Mismatch

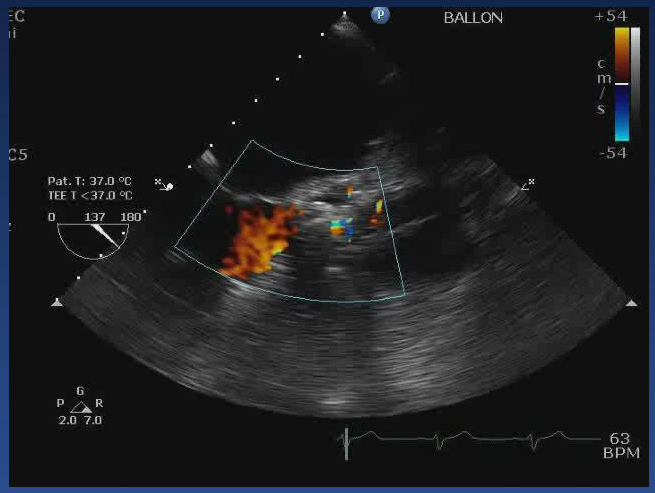
Size Mismatch

- Severe paravalvular leak following implantation in large annulus
- Proper valve sizing is CRITICAL to avoid mismatch and severe PV leak

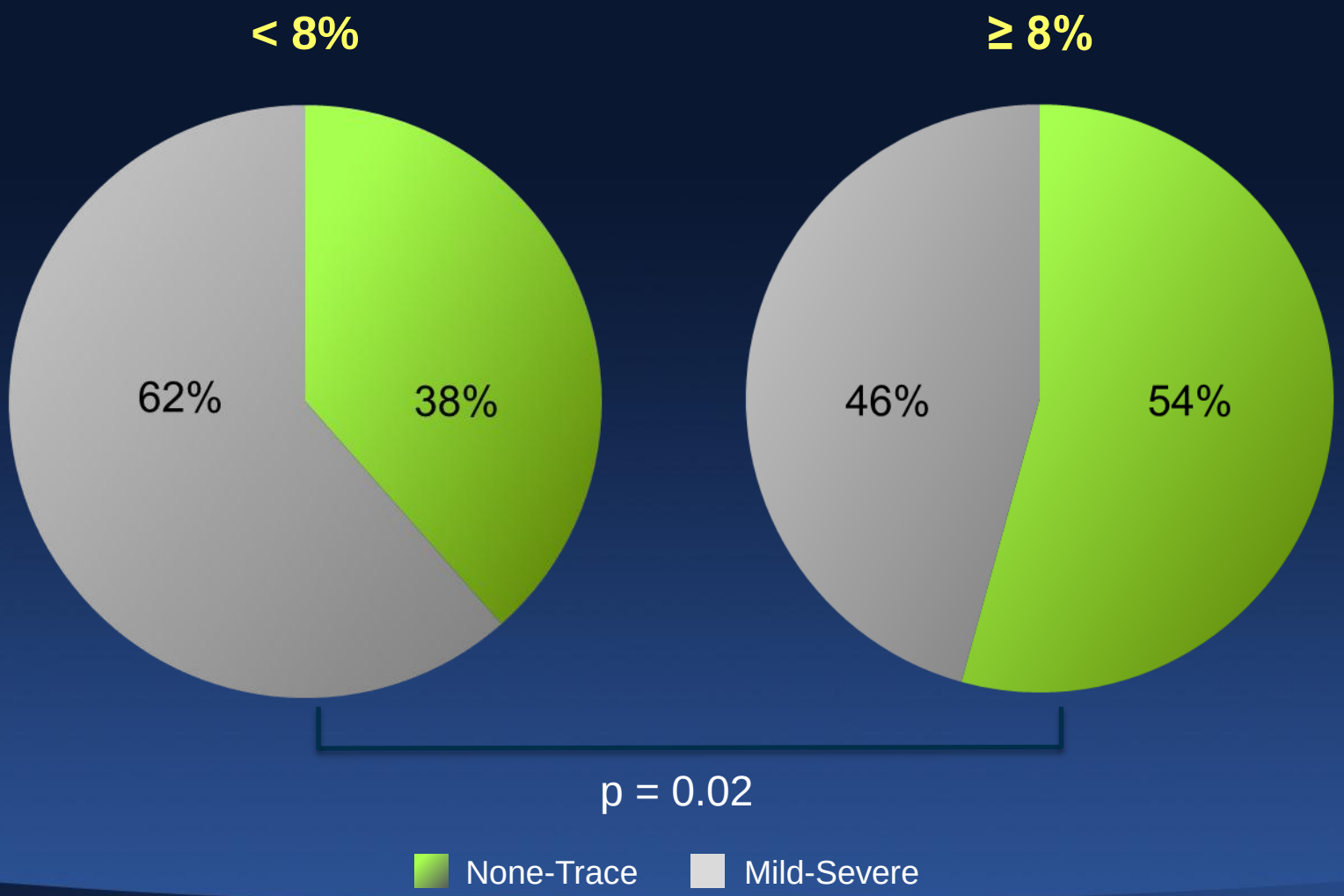
Management

- Pressors to stabilize hemodynamics
- If patient unstable, consider surgical AVR
- *Cannot* put larger valve inside of smaller valve





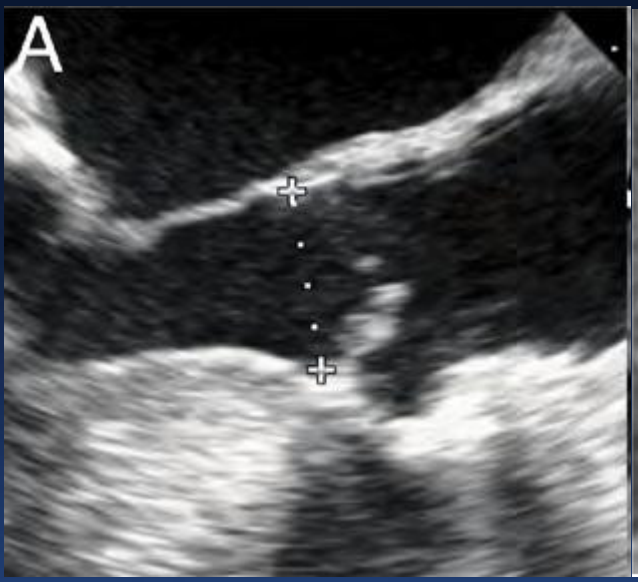
Paravalvular Leak by Cover Index
PARTNER Trial – Cohort A

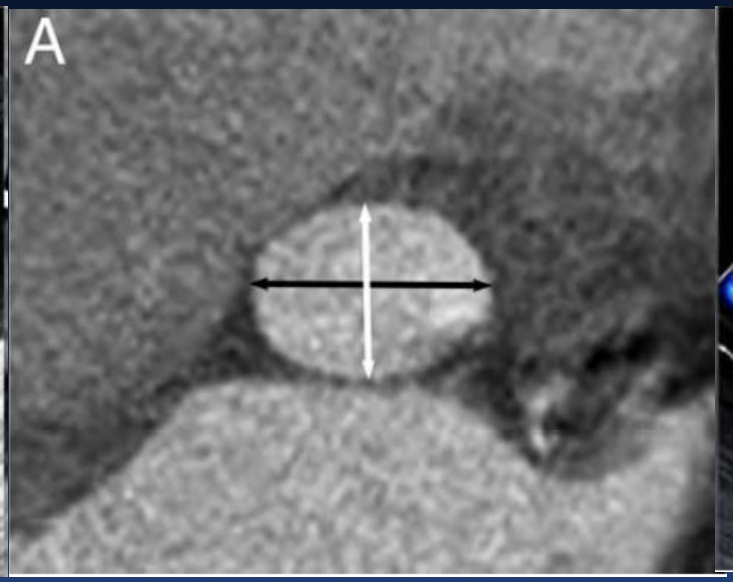


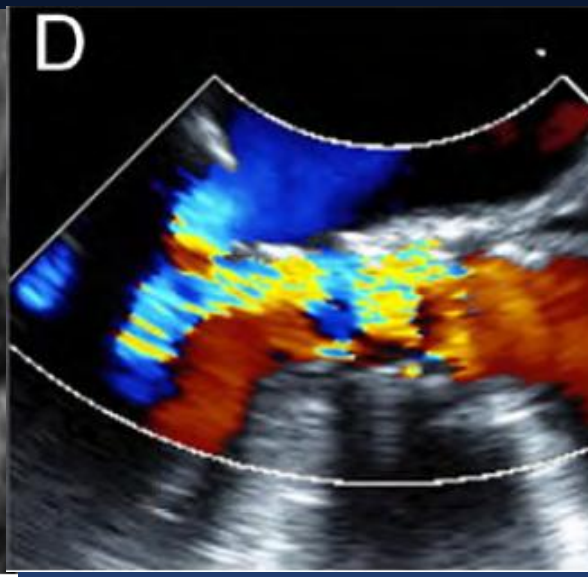
Cover index = 100X [(valve diameter - annulus diameter) ÷ valve diameter]

Valve Undersizing

2D TEE (22 mm) **CT (22×28 mm)** **TEE Post**



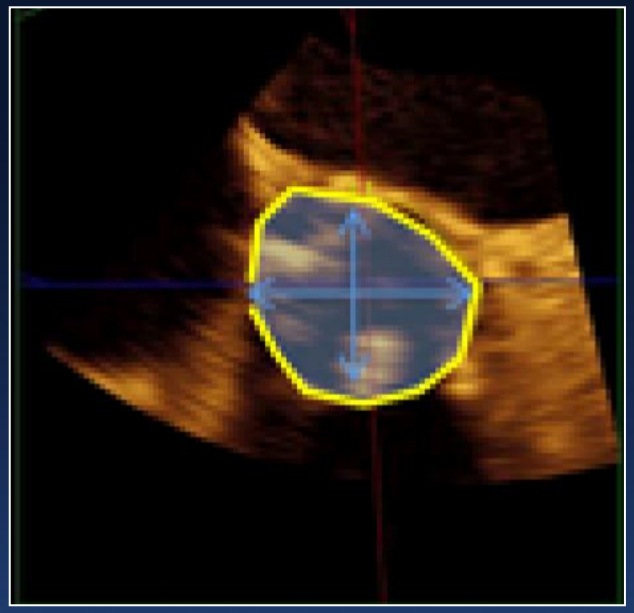




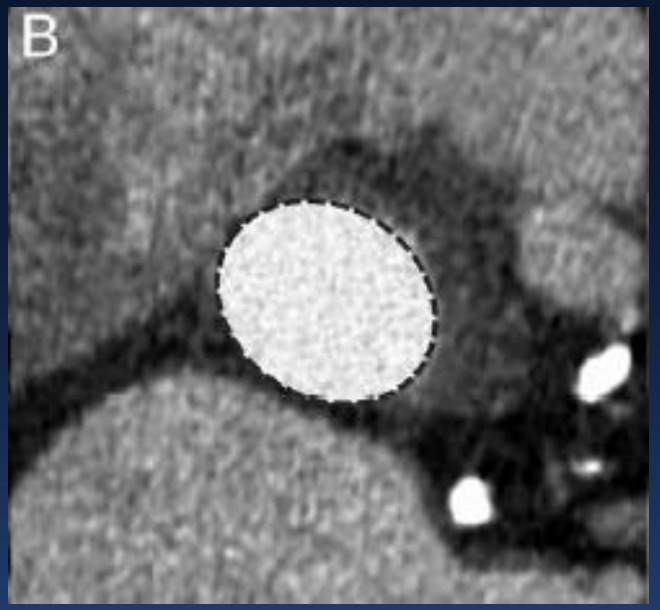
Wilson et al., JACC 2012

3D Imaging is Key!

3D TEE



CT

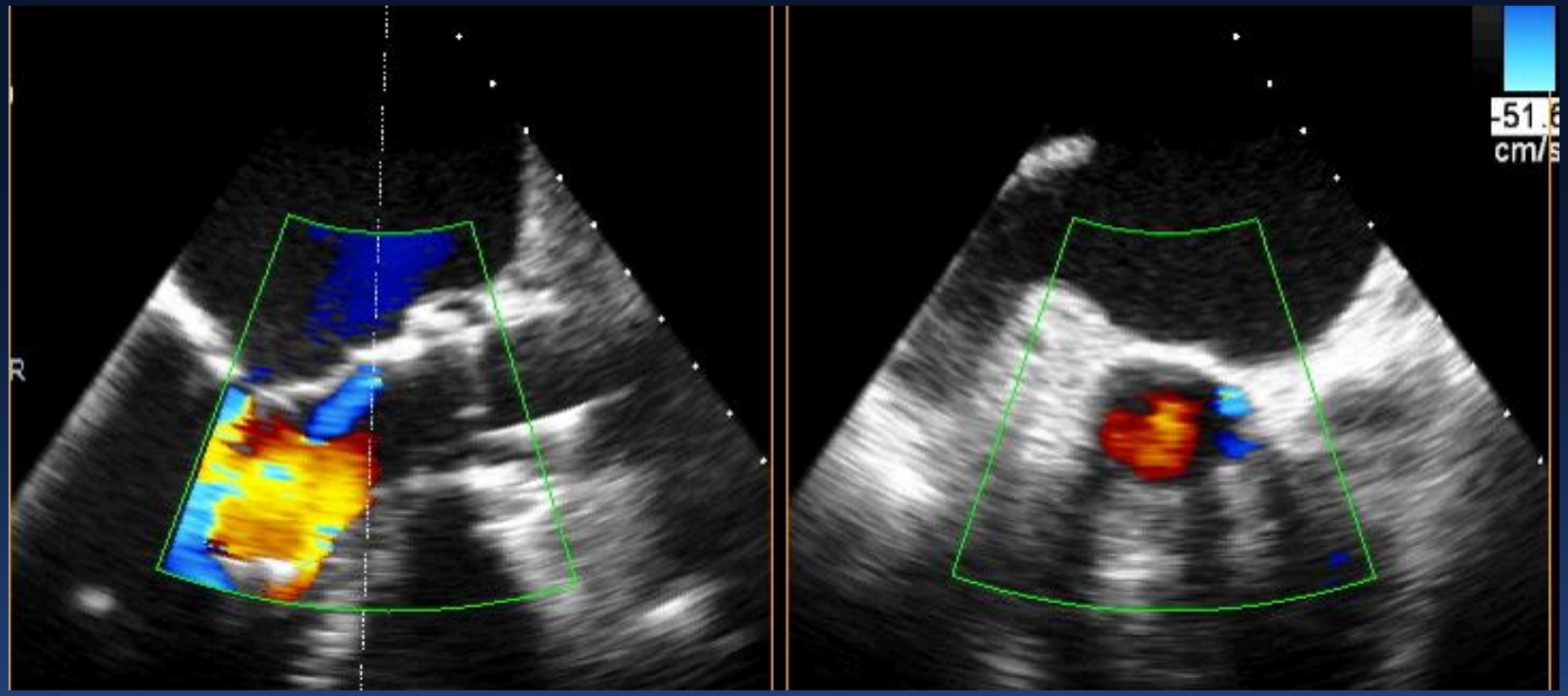


Average annular diameter = circumference / π

Oversize average annular diameter by 1 mm

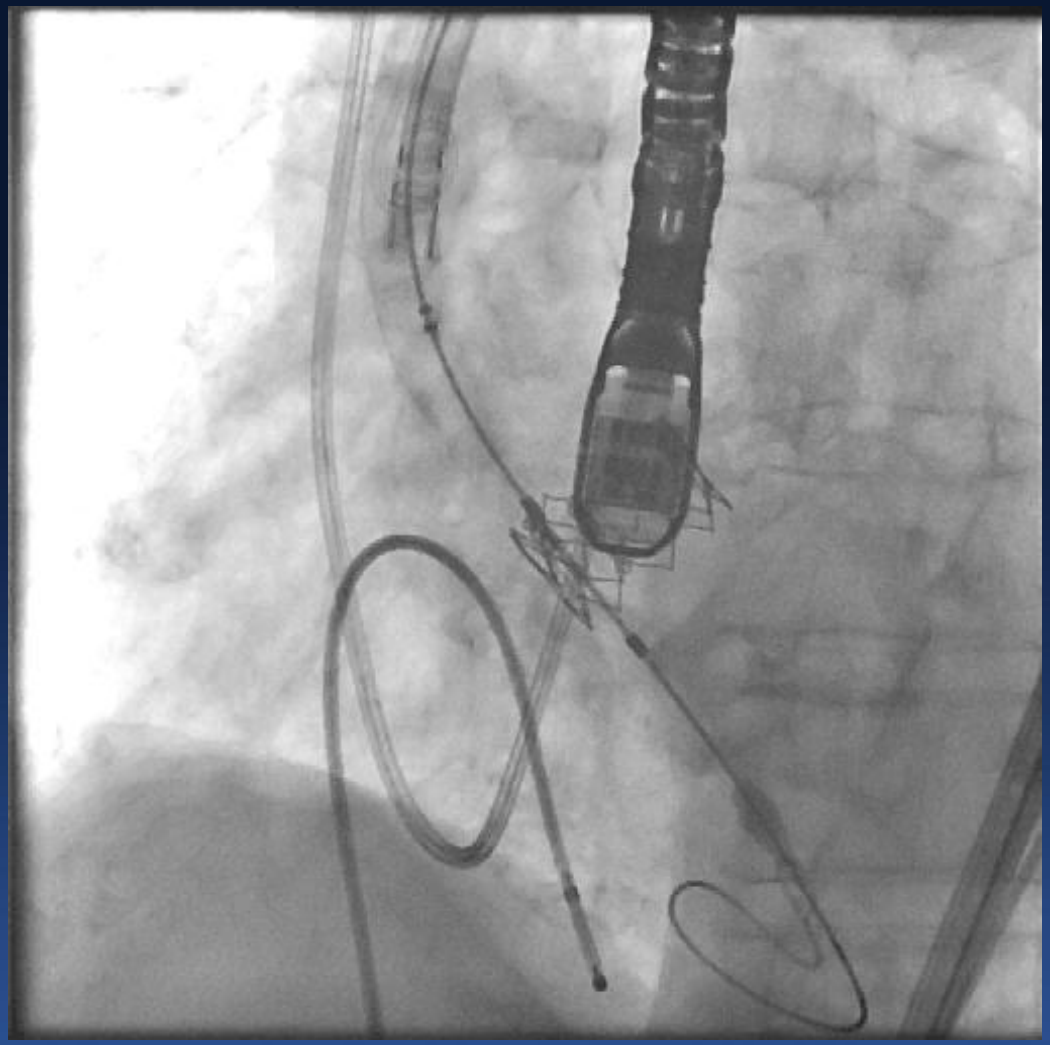
Role of Balloon Post-Dilatation

Case example



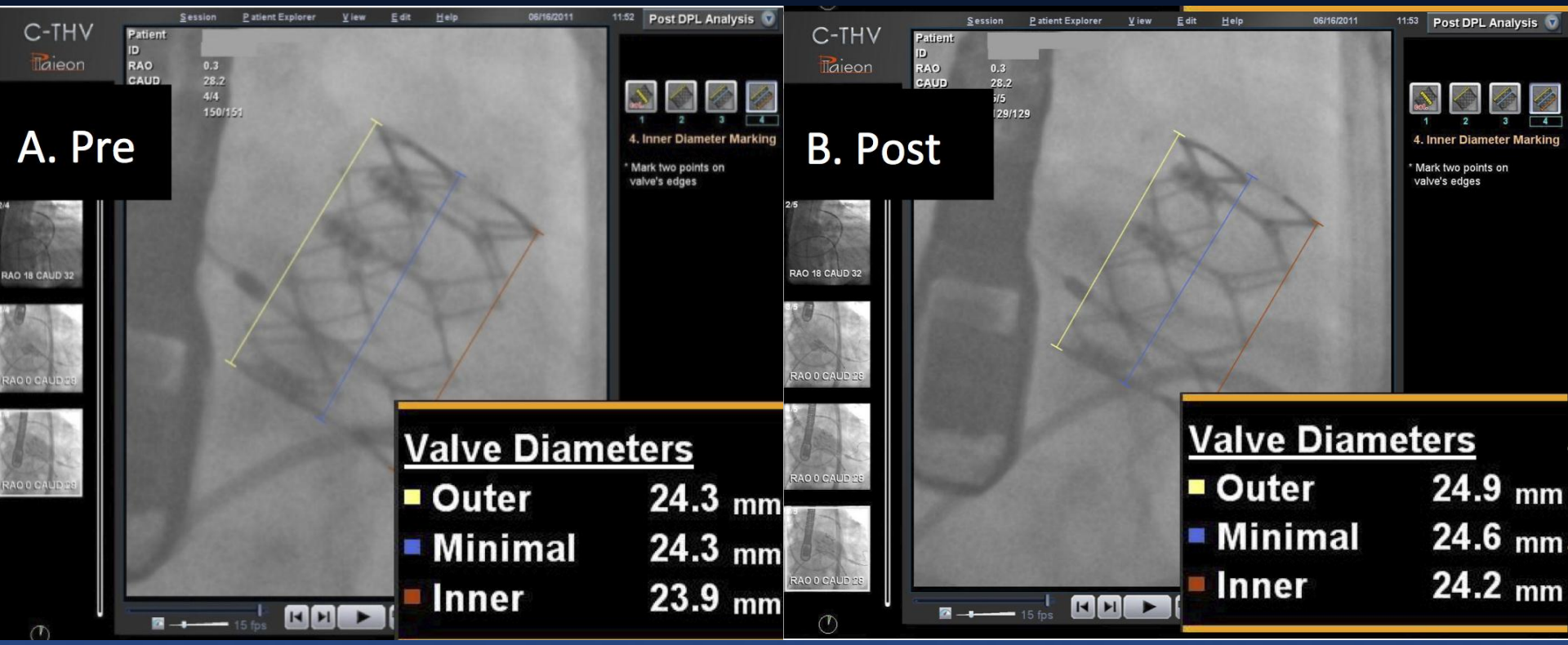
Role of Balloon Post-Dilatation

Case example



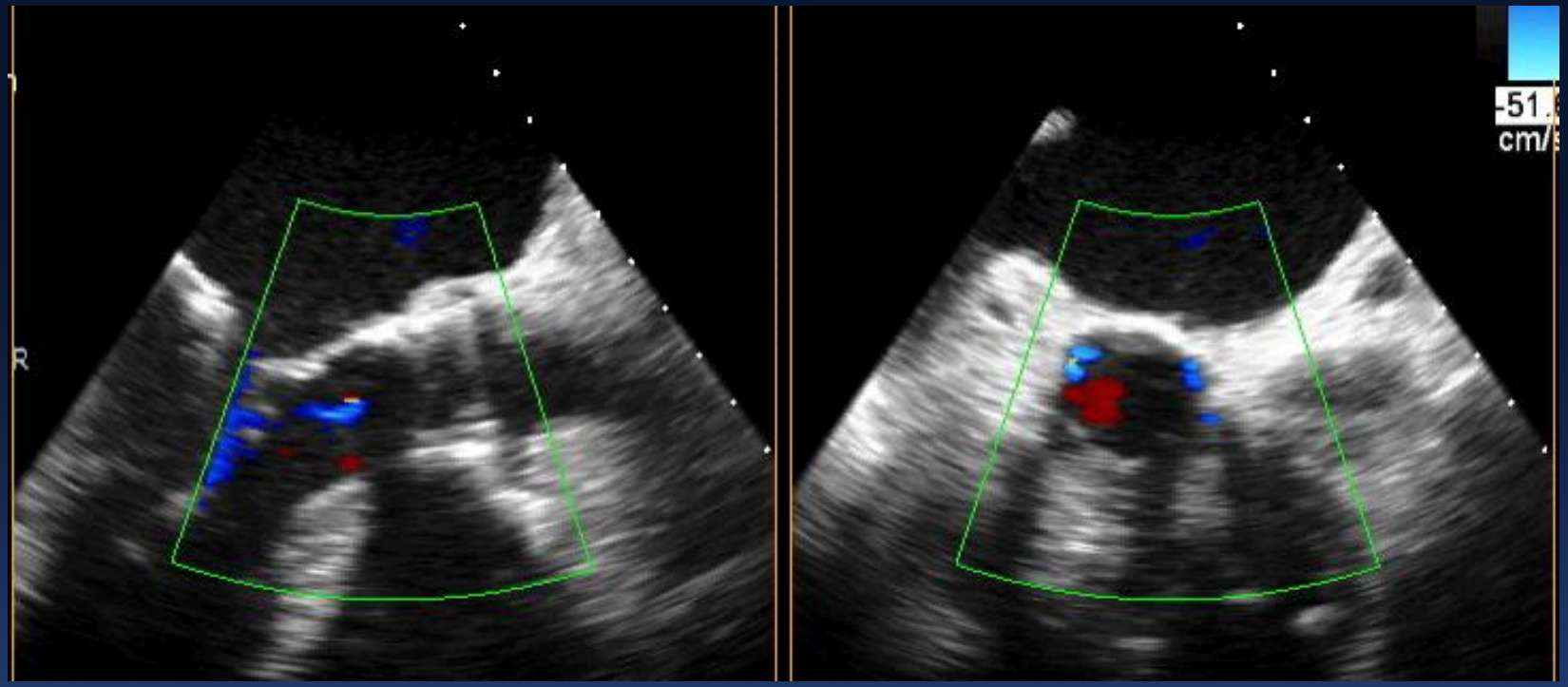
Balloon post-dilatation performed with addition of 1cc to delivery catheter

Additional stent expansion after PD



Role of Balloon Post-Dilatation

Case example



Risk	Benefit
• Central AR • Aortic trauma • Embolic complications	• Reduce paravalvular AR • Improved THV shape/hemodynamics

Outcomes Following Post-Dilatation

Columbia Experience

Baseline characteristics

	Post dilatation N = 106	No Post dilatation N =153	P value
Male gender	67%	40%	<0.001
Age (year)	85.4 ± 8.0	85.8 ± 7.3	0.66
STS score	10.7 ± 4.6	12.1 ± 4.4	0.01
Weight (kg)	73.0 ± 17.3	66.1 ± 17.2	0.002
Height (cm)	167.8 ± 11.3	160.6 ± 10.8	<0.001
BMI	25.8 ± 5.3	25.6 ± 6.4	0.76
BSA (m^2)	1.75 ± 0.42	1.66 ± 0.30	0.06

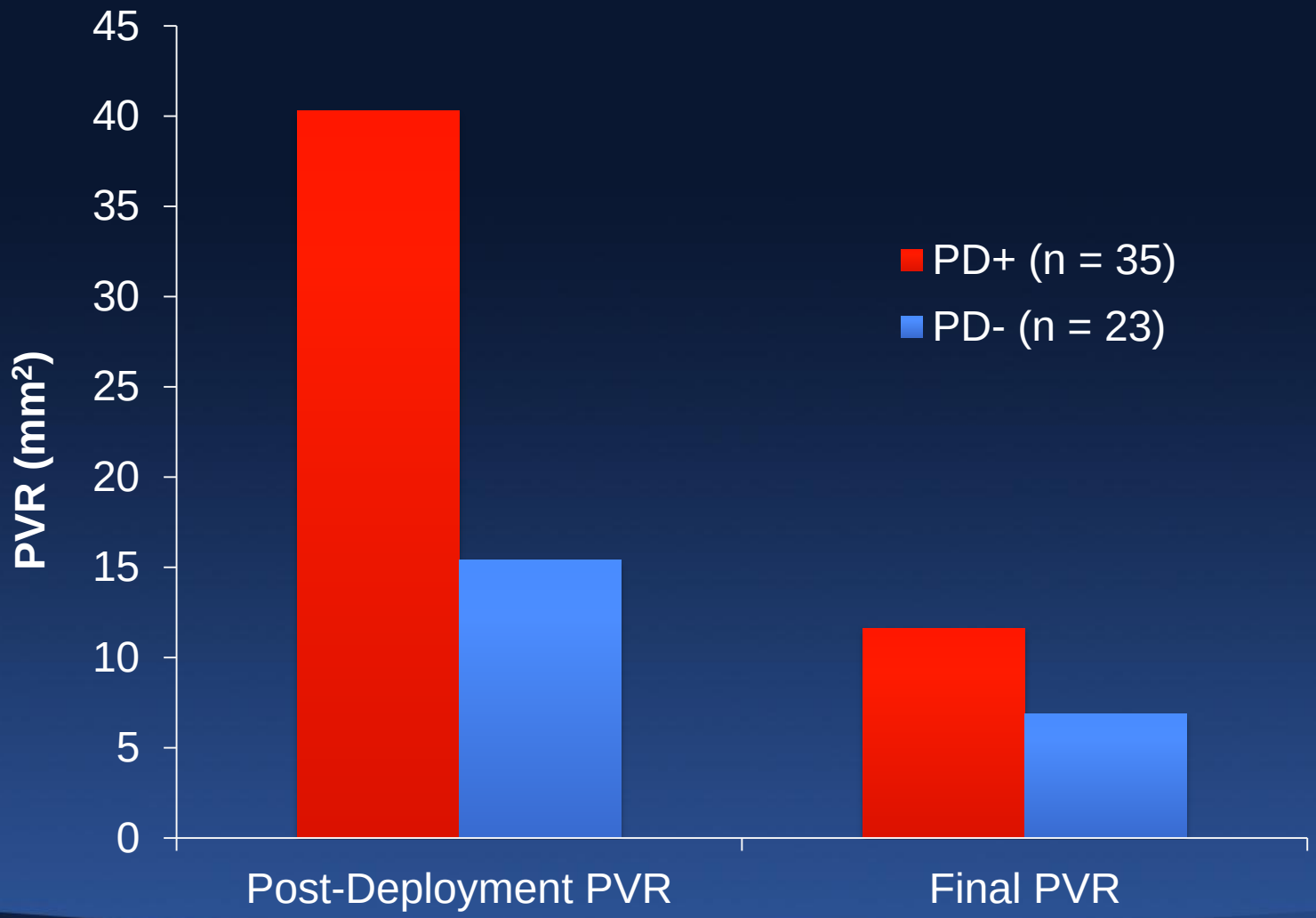
Outcomes Following Post-Dilatation

Columbia Experience

Echocardiographic characteristics

	Post dilatation N = 106	No Post dilatation N =153	P value
Ejection fraction (%)	47.0 ± 16.2	50.2 ± 14.4	0.11
AVA (cm^2)	0.61 ± 0.17	0.58 ± 0.17	0.08
AVA index (cm^2/m^2)	0.34 ± 0.09	0.34 ± 0.09	0.73
Mean aortic gradient (mmHg)	45.5 ± 12.1	46.4 ± 14.2	0.59
Annulus diameter - TEE (mm)	23.3 ± 1.8	22.0 ± 1.9	< 0.001
Cover-index	7.4 ± 4.8	10.2 ± 5.1	< 0.001

PVR Decreased by Post-Dilatation



Outcomes Following Post-Dilatation

Columbia Experience

Clinical Outcomes

	Post dilatation N = 106	No Post dilatation N =153	OR (95%CI)	P value
30-day mortality	2 (1.9%)	11 (7.2%)	0.25 (0.05-1.14)	0.06
30-day cardiac mortality	1 (0.9%)	6 (3.9%)	0.23 (0.03-1.97)	0.25
In-hospital cerebrovascular events				
All stroke or TIA	5 (4.7%)	2 (1.3%)	3.74 (0.71-19.64)	0.13
All stroke	4 (3.8%)	1 (0.7%)	5.96 (0.66-54.10)	0.16
Aortic dissection	1 (0.9%)	1 (0.7%)	1.45 (0.09-23.4)	1.00
Aortic wall hematoma	1 (0.9%)	3 (2.0%)	0.48 (0.05-4.64)	0.65
PPM implantation during index hospitalization	6 (5.7%)	13 (8.5%)	0.65 (0.24-1.76)	0.39

Outcomes Following Post-Dilatation

Columbia Experience

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CLINICAL STUDIES

Predictive Factors, Efficacy, and Safety of Balloon Post-Dilation Following Transcatheter Aortic Valve Implantation With a Balloon-Expandable Valve

Luis Nombela-Franco, MD, Josep Rodés-Cabau, MD, Robert Delarochellière, MD, Eric Larose, MD, Daniel Doyle, MD, Jacques Villeneuve, MD, Sébastien Bergeron, MD, Mathieu Bernier, MD, Ignacio Amat-Santos, MD, Michael Mok, MD, Marina Urena, MD, Michel Rheault, MD, Jean Dumesnil, MD, Mélanie Côté, MSc, Philippe Pibarot, PHD, Eric Dumont, MD

Quebec City, Quebec, Canada

Objectives This study sought to evaluate the predictive factors, effects, and safety of balloon post-dilation (BPD) for the treatment of significant paravalvular aortic regurgitation (AR) following transcatheter aortic valve implantation (TAVI).

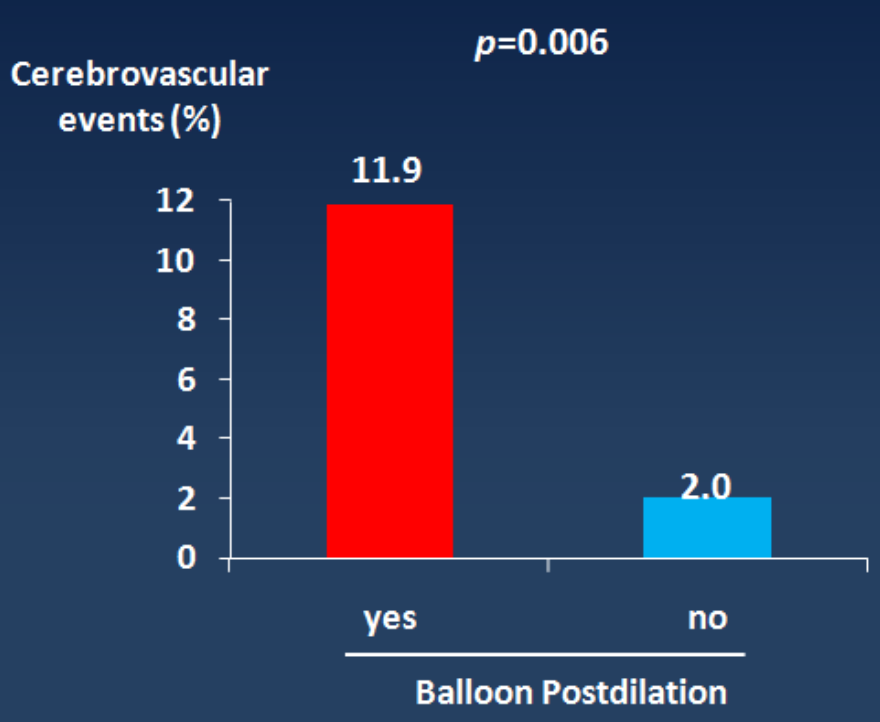
Background Very few data exist on BPD following TAVI with a balloon-expandable valve.

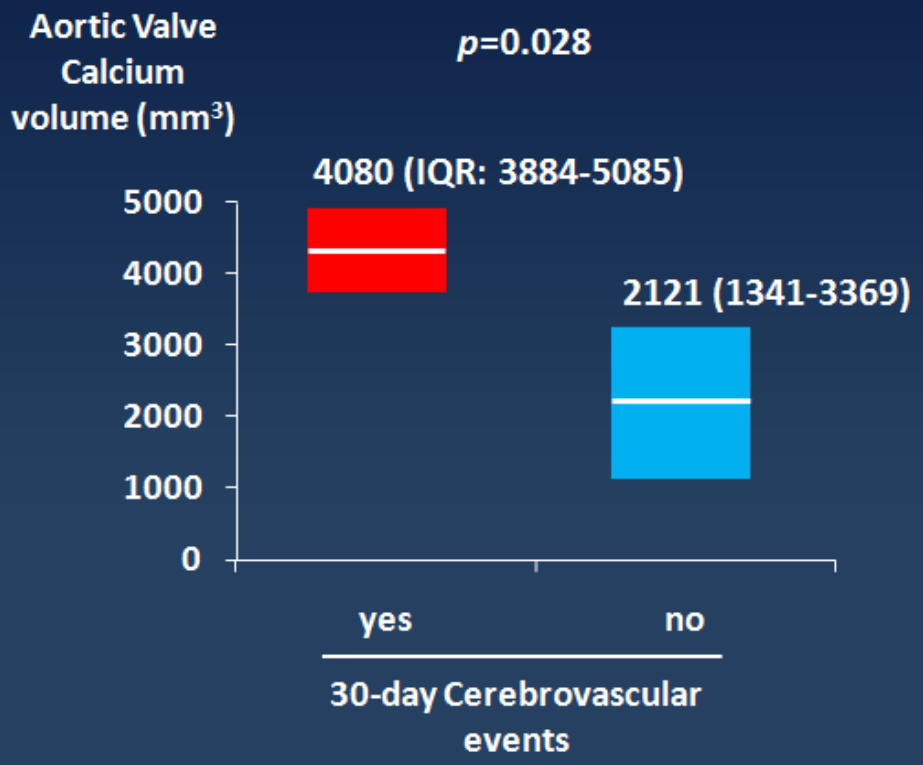
Methods A total of 211 patients who underwent TAVI with a balloon-expandable valve were included. BPD was performed after TAVI if paravalvular AR ≥2 was identified by transesophageal echocardiography. Clinical events and echocardiographic data were prospectively recorded, and median follow-up was 12 (6 to 24) months.

Results BPD was performed in 59 patients (28%), leading to a reduction in at least 1 degree of AR in 71% of patients, with residual AR <2 in 54% of the patients. The predictors of the need for BPD were the degree of valve calcification and transfemoral approach, with valve calcification volume >2,200 and >3,800 mm^3 best determining the need for and a poor response to BPD, respectively. Patients who underwent BPD had a higher incidence of cerebrovascular events at 30 days (11.9% vs. 2.0%, p = 0.006), with most (83%) events within the 24 h following the procedure occurring in patients who had BPD. No significant changes in valve area or AR degree were observed at follow-up in BPD and no-BPD groups.

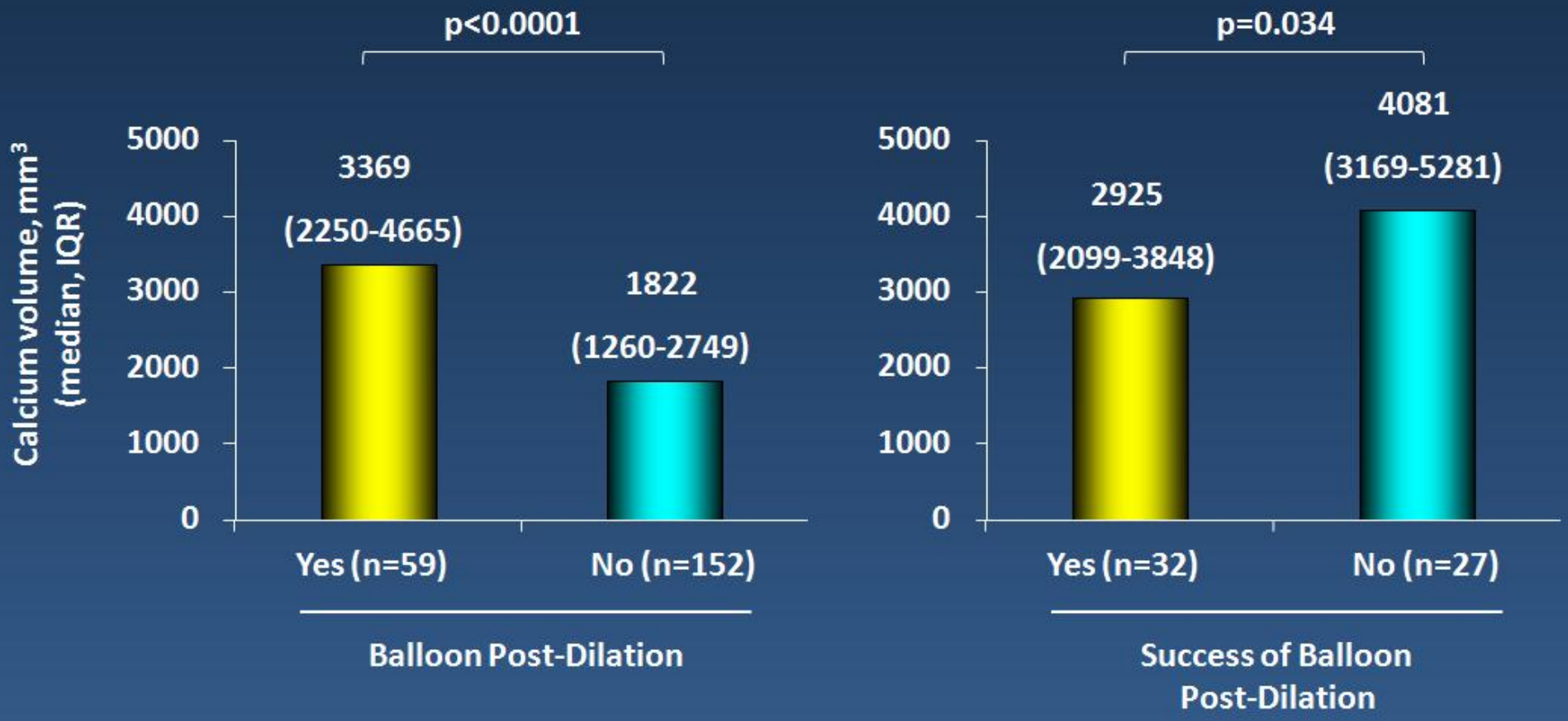
Conclusions BPD was needed in about one-fourth of the patients undergoing TAVI with a balloon-expandable valve and was successful in about one-half of them. A higher degree of valve calcification and transfemoral approach predicted the need for BPD. BPD was not associated with any deleterious effect on valve function at mid-term follow-up, but a higher rate of cerebrovascular events was observed in patients who had BPD. (J Am Coll Cardiol Intv 2012;xx:xxx) © 2012 by the American College of Cardiology Foundation

30-Day Cerebrovascular Events (stroke: 4.3%)





Valve calcium volume according to balloon post-dilatation and to the success of balloon post-dilation



Conclusions

- Post-procedural AR, was more common after TAVR (mild-mod-severe ~50%) and did not change significantly during follow-up
- Even mild post-procedural AR (paravalvular and total AR) was associated with increased subsequent mortality
- Valve in valve is a potential treatment option for AR due to malpositioning
- Balloon post-dilatation improves regurgitant volume but may result in increased neurologic events