

# PVR After TAVR: Insights from PARTNER II S3HR and S3i

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# Disclosure Statement of Financial Interest

## Susheel K. Kodali, MD

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

- Honoraria
- Steering Committee
- SAB

### Company

- St. Jude Medical, Claret Medical
- Edwards Lifesciences, Claret Medical
- Thubrikar Aortic Valve, Inc, Dura Biotech, VS Medtech

# Incidence, Predictors, and Outcomes of Aortic Regurgitation After Transcatheter Aortic Valve Replacement

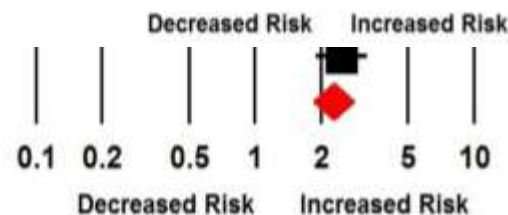
Meta-Analysis and Systematic Review of Literature

Ganesh Athappan, MD,\*† Eshan Patvardhan, MD,\* E. Murat Tuzcu, MD,\*  
 Lars Georg Svensson, MD, PhD,‡ Pedro A. Lemos, MD,§ Chiara Fraccaro, MD, PhD,||  
 Giuseppe Tarantini, Davide Capodanno, Antonio Colombo, |

## Impact of Mild AR on Mortality

Study name	Statistics for each study					Hazard ratio and 95% CI
	Hazard ratio	Lower limit	Upper limit	Z-Value	p-Value	
Lemos	10.080	1.229	82.673	2.152	0.031	
Sinning	2.342	1.066	5.145	2.119	0.034	
Kodali	2.110	1.433	3.107	3.782	0.000	
Fraccaro	2.064	0.968	4.400	1.876	0.061	
Tamburino	0.780	0.499	1.218	-1.092	0.275	
<b>All (N=1620)</b>	<b>1.829</b>	<b>1.005</b>	<b>3.329</b>	<b>1.975</b>	<b>0.048</b>	

Gilard	2.490	1.909	3.248	6.728	0.000	
<b>All (N=4791)</b>	<b>2.273</b>	<b>1.840</b>	<b>2.808</b>	<b>7.609</b>	<b>0.000</b>	

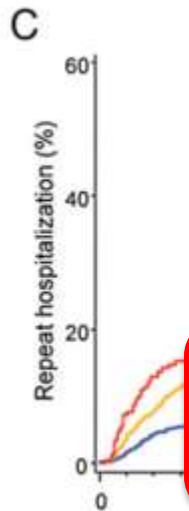


# Paravalvular regurgitation after transcatheter aortic valve replacement with the Edwards sapien valve in the PARTNER trial: characterizing patients and impact on outcomes

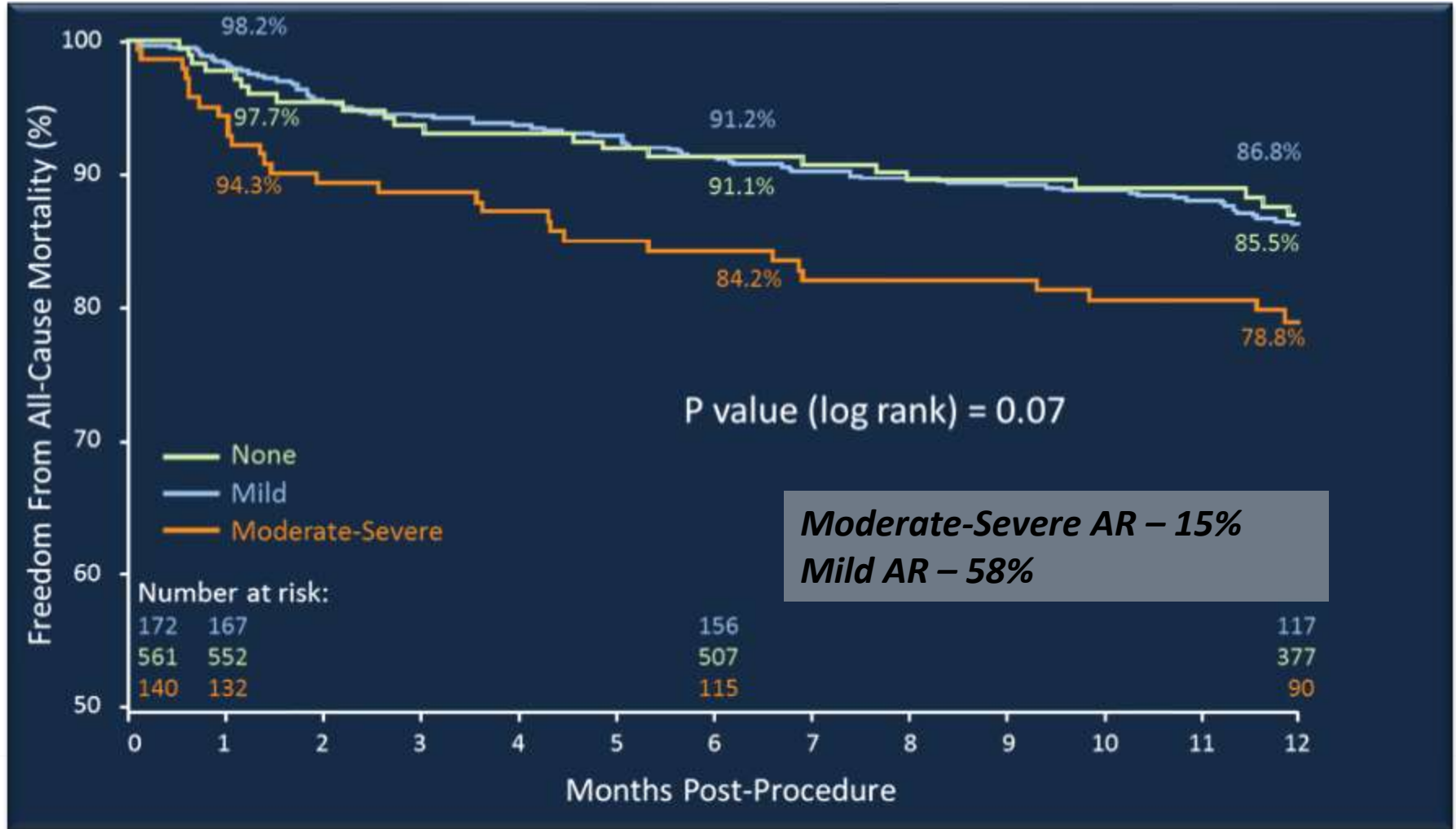
Susheel Kodali<sup>1\*</sup>, Philippe Pibarot<sup>2</sup>, Pamela S. Douglas<sup>3</sup>, Mathew Williams<sup>1</sup>, Ke Xu<sup>4</sup>, Vinod Thourani<sup>5</sup>, Charanjit S. Rihal<sup>6</sup>, Alan Zajarias<sup>7</sup>, Darshan Doshi<sup>1</sup>, Michael Davidson<sup>8</sup>, E. Murat Tuzcu<sup>9</sup>, William Stewart<sup>9</sup>, Neil J. Weissman<sup>10</sup>, Lars Svensson<sup>9</sup>, K. Martin B. Leon<sup>1</sup>, a

Multivariable Analysis – Baseline and Procedural Predictors of One Year Mortality

Variable	Hazard Ratio	95% Confidence Interval	p-value
Major Arrhythmia	1.41	1.13-1.76	0.0024
TF vs. TA	0.74	0.59-0.92	0.008
AV Annulus Diameter (per 1 mm increase)	1.06	1.02-1.11	0.002
BMI (per 1 kg/m <sup>2</sup> increase)	0.95	0.93-0.97	<0.0001
Total Distance Walked (per 10m increase)	0.97	0.96-0.98	<0.0001
LV Mass (per 10g increase)	1.02	1.00-1.03	0.035
AV Mean Gradient (per 1 mmHg)	0.98	0.97-0.99	<0.0001
Paravalvular Regurgitation			
None/Trace	Referent	-	-
Mild	1.37	1.07-1.76	0.012
Moderate/Severe	2.18	1.57-3.02	<0.0001
Renal disease (CR ≥=2)	1.39	1.08-1.80	0.012
Baseline Moderate/Severe Total AR	0.85	0.60-1.20	0.351

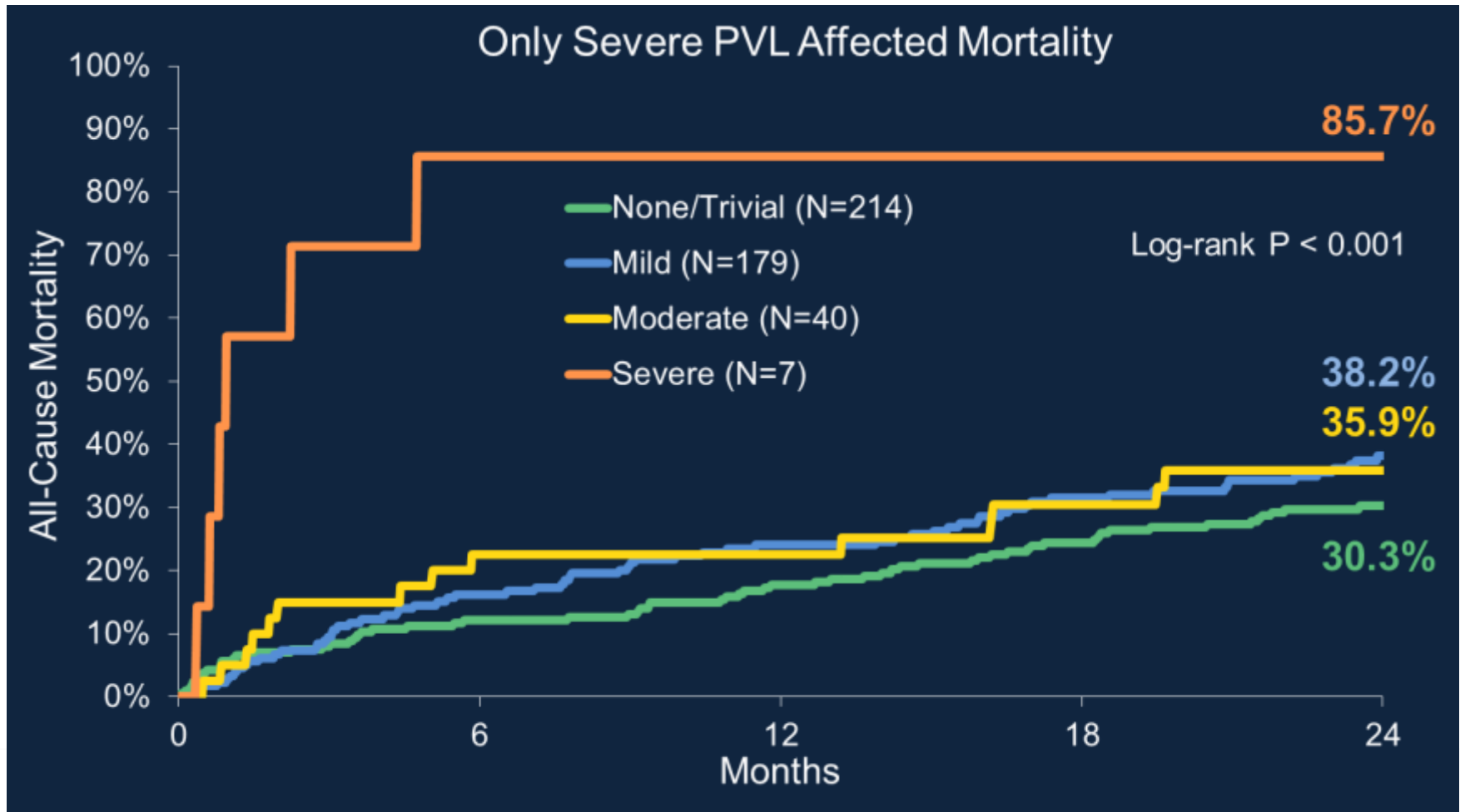


# CoreValve ADVANCE | Survival by AR\*



\*At discharge

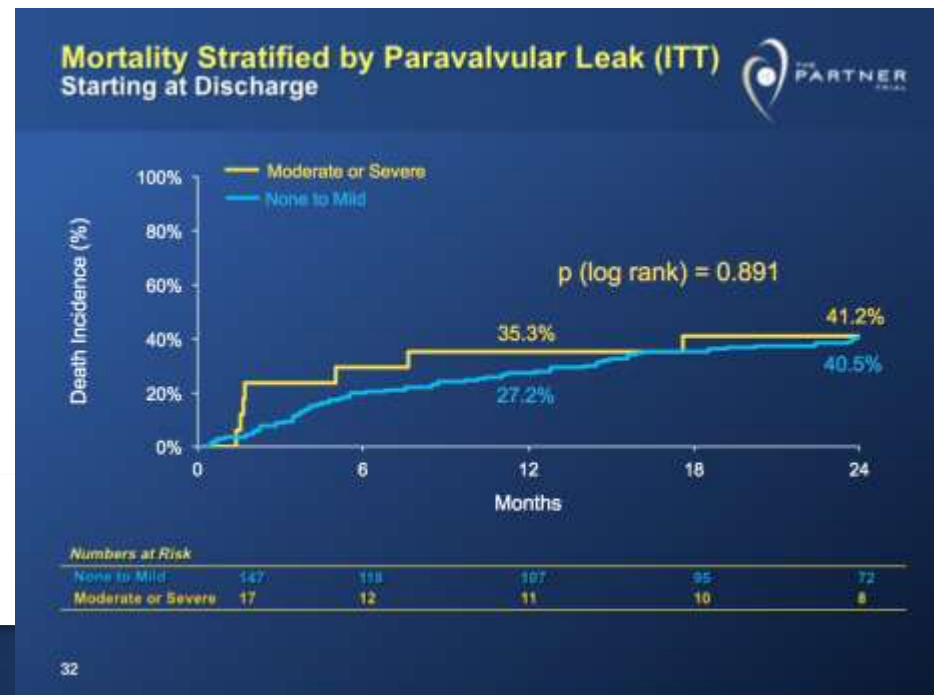
# PVL and All-Cause Mortality (CoreVALVE Extreme Risk)





# *Why is there conflicting data regarding mild PVL and its impact on mortality?*

- Different patient populations – Competing Risks

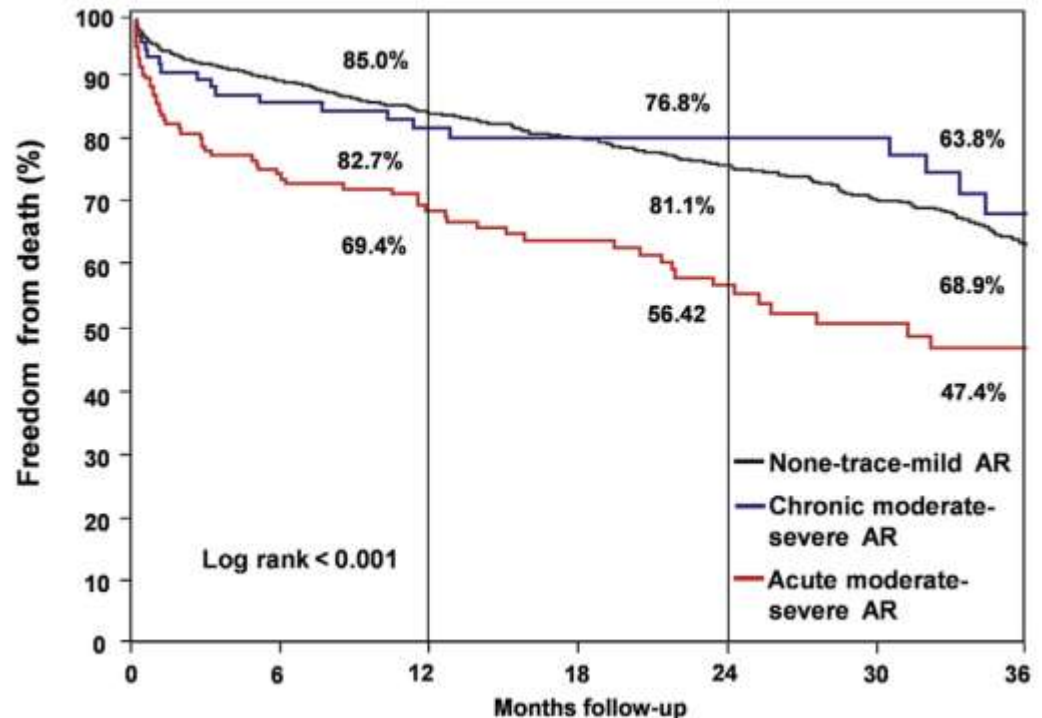


# Clinical Impact of Aortic Regurgitation After Transcatheter Aortic Valve Replacement

## Insights Into the Degree and Acuteness of Presentation

Miguel Jerez-Valero, MD,\* Marina Urena, MD,\* John G. Webb, MD,† Corrado Tamburino, MD,‡  
 Antonio J. Munoz-Garcia, MD, PhD,§ Asim Cheema, MD,|| Antonio E. Dager, MD,¶ Vicenç Serra, MD,#  
 Ignacio J. Amat-Santos, MD,\*\* Marco Barbanti, MD,†† Sebastiano Immè, MD,‡‡ Juan H. Alonso Briales, MD,§§  
 Hatim Al Lawati, MD,||| Luis Miguel Benitez, MD,¶¶ Angela Maria Cucalon, MD,¶¶¶ Bruno Garcia del Blanco, MD,¶¶¶  
 Ana Revilla, MD, PhD,\*\* Eric Dumont, MD,\* Henrique Barbosa,  
 Sébastien Bergeron, MD,\* Philippe Pibarot, PhD,\* Josep Rodés

- Registry of 1735 patients
- Moderate to Severe PVR present in 14.2% of patients
- Although mild PVL did not impact late mortality, moderate PVL did lead to worse survival (HR – 1.68[1.27-2.24])
- Magnitude of impact blunted by presence of baseline AR





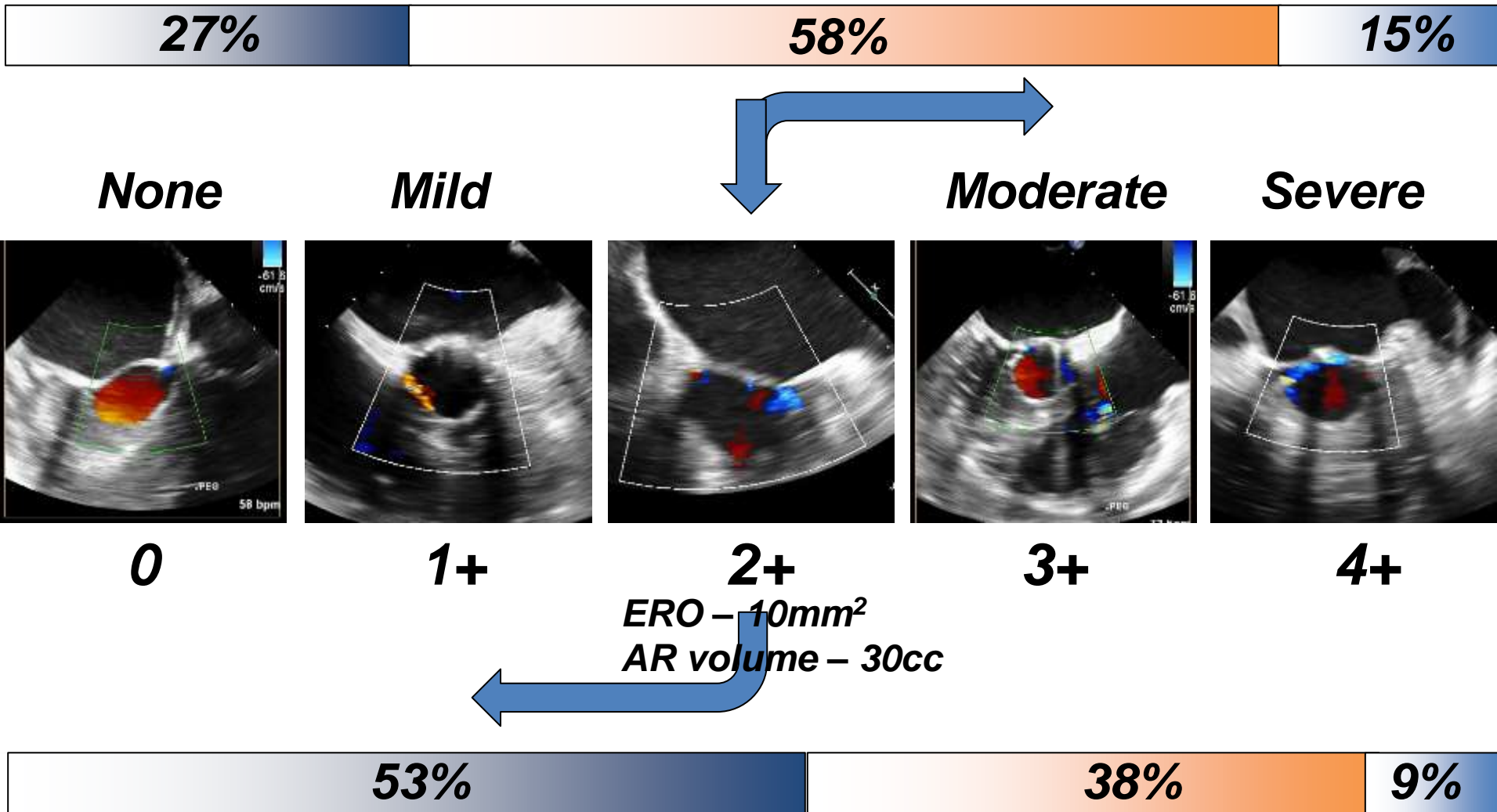
# *Why is there conflicting data regarding mild PVL and its impact on mortality?*

- Different patient populations – Competing Risks
- Differential impact based on valve type (PVR regression over time with CoreValve?)

# *Why is there conflicting data regarding mild PVL and its impact on mortality?*

- Different patient populations – Competing Risks
- Differential impact based on valve type (PVR regression over time with CoreValve?)
- Challenges with assessment

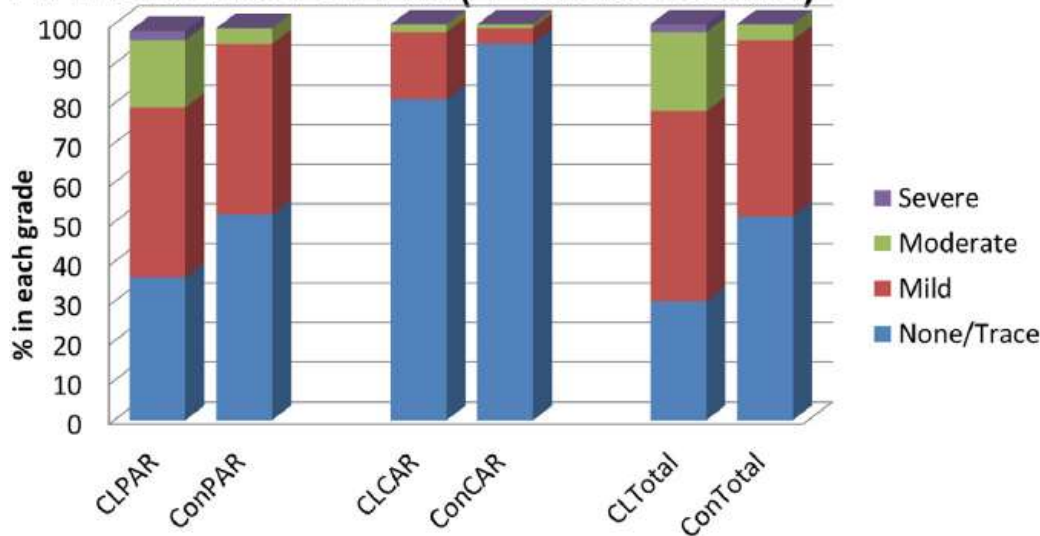
# Challenges of PVL Assessment



# Assessment of Paravalvular Aortic Regurgitation after Transcatheter Aortic Valve Replacement: Intra-Core Laboratory Variability

Rebecca T. Hahn, MD, FACC, Philippe Pibarot, DVM, PhD, FACC, Neil J. Weissman, MD, FACC, Leonardo Rodriguez, MD, FACC, and Wael A. Jaber, MD, FACC, *New York, New York; Québec City, Québec, Canada; Washington, District of Columbia; and Cleveland, Ohio*

## A. Incidence of AR (4-Grade Scale)



**15.9% of patients graded as moderate by one corelab would be graded as mild by another corelab consortium**

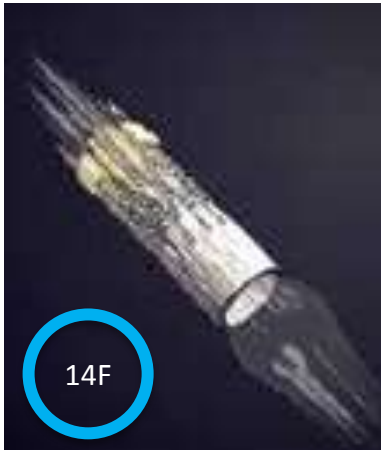
**Table 2** Number of patients in each PAR grade for the PARTNER IIB core laboratory and the consortium: four-grade scale

PARTNER IIB core laboratory	Consortium			
	1	2	3	4
1	31*	1 <sup>†</sup>	0	0
2	17 <sup>‡</sup>	21*	0	0
3	0	14 <sup>‡</sup>	1*	0
4	0	0	2 <sup>‡</sup>	0*

PAR, Paravalvular aortic regurgitation.  
 Grading scheme: 1 = none/trace; 2 = mild; 3 = moderate; 4 = severe.  
 \*Agreement between core laboratory and consortium.  
<sup>†</sup>Underestimation by the core laboratory.  
<sup>‡</sup>One-grade overestimation by the core laboratory.

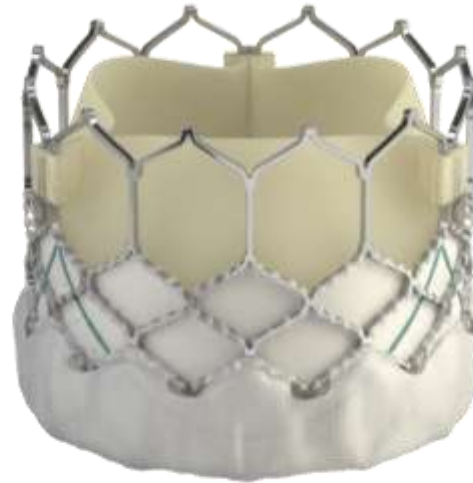
# SAPIEN 3 Transcatheter Heart Valve

## Distinguishing Features



### LOW PROFILE ACCESS

- 14F eSheath compatible\*



### VALVE DESIGN

- Balloon Expandable
- Bovine Pericardial Tissue
- Outer Sealing Skirt

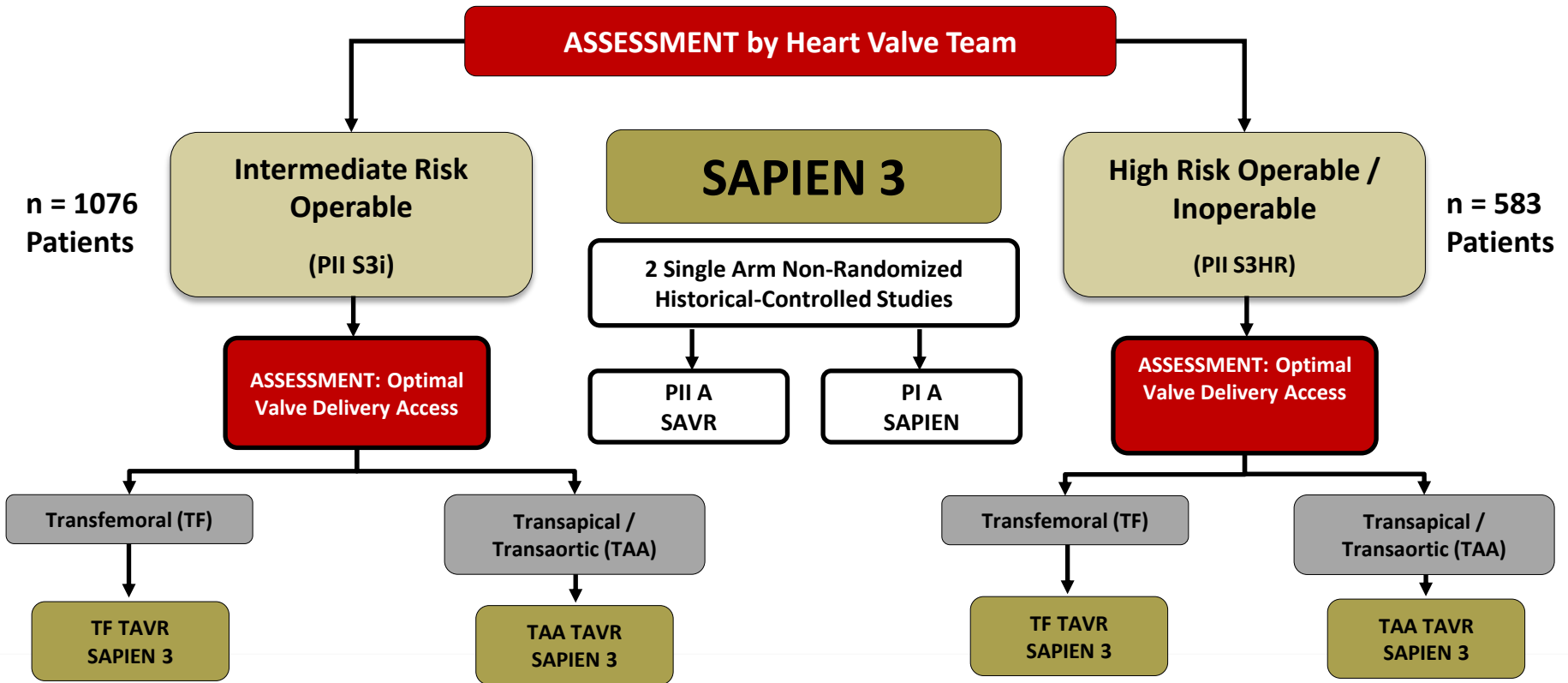


### ACCURATE PLACEMENT

- Distal flex & fine adjustment feature
- Center Marker Positioning

# The PARTNER II S3 Trial Study Design

Symptomatic Severe Aortic Stenosis

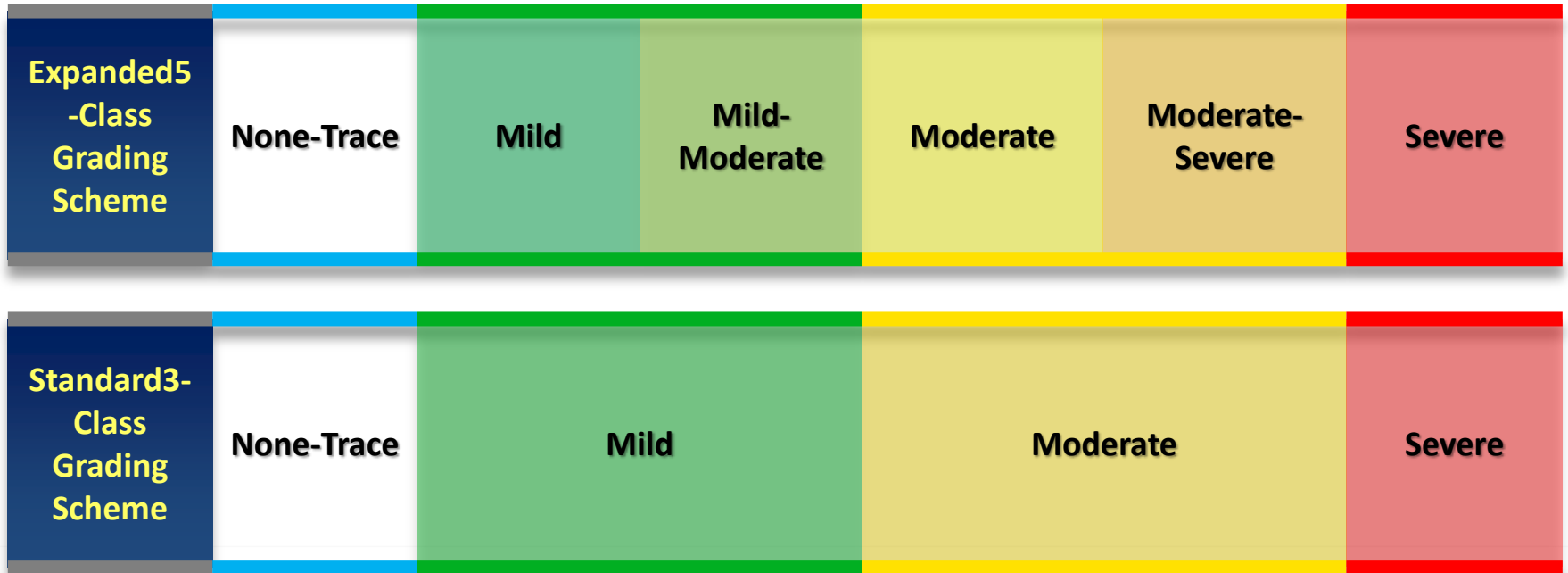




# Echo PVR Methodology

## Grading Scales

Echo assessment of paravalvular regurgitation based on an expanded classification scheme which was then collapsed to the standard classification scheme



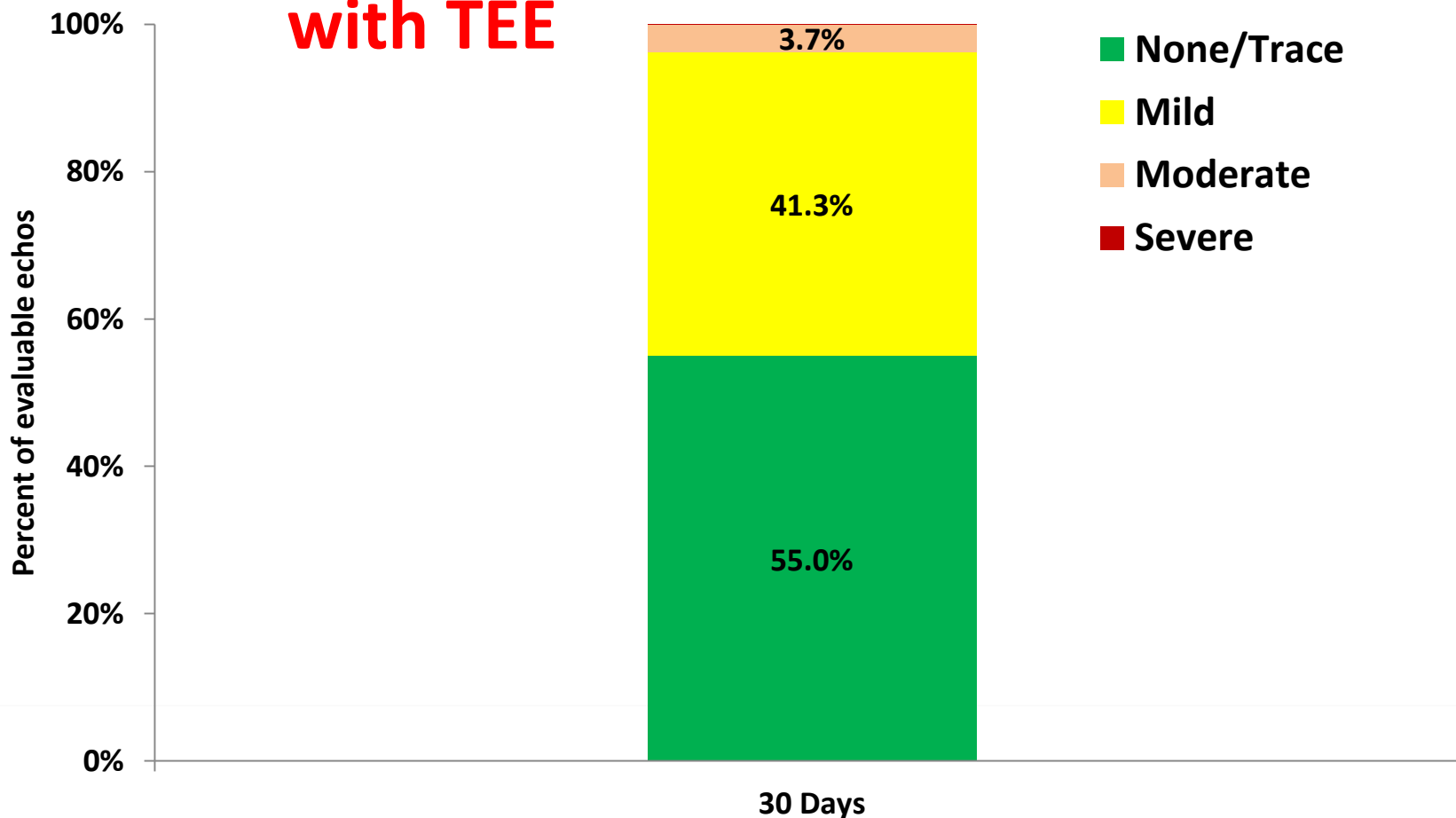
# Echo PVR Methods

## Grading Scales

3-CLASS GRADING SCHEME	TRACE	MILD		MODERATE		SEVERE
UNIFYING 5-CLASS GRADING SCHEME	TRACE	MILD	MILD-TO-MODERATE	MODERATE	MODERATE-TO-SEVERE	SEVERE
<b>Structural Parameters</b>						
• Valve stent	Usually normal	Usually normal	Normal/abnormal†	Normal/abnormal†	Usually abnormal†	Usually abnormal†
<b>Doppler parameters (qualitative or semi-quantitative)</b>						
• Jet features						
Extensive/wide jet origin	Absent	Absent	Absent	Present	Present	Present
Multiple jets	Possible	Possible	Often present	Often present	Usually present	Usually present
Jet path visible along the stent	Absent	Absent	Possible	Often present	Usually present	Present
Proximal Flow convergence visible	Absent	Absent	Absent	Possible	Usually present Often present	Often present
• Jet width at its origin (%LVOT diameter): color Doppler	Narrow (<5)	Narrow (5-15)	Intermediate (15-30)	Intermediate (30-45)	Large (45-60)	Large (>60)
○ Jet deceleration rate (PHT, ms): CW Doppler	Slow (>500)	Slow (>500)	Slow (>500)	Variable (200-500)	Variable (200-500)	Steep (<200)
○ Diastolic flow reversal in the descending aorta: PW Doppler	Absent	Absent or brief early diastolic	Intermediate	Intermediate	Holodiastolic (end-diast. vel.>20 cm/s)	Holodiastolic (end-diast. vel.>25 cm/s)
• Circumferential extent of PVR (%) color Doppler	<10	<10	10-20	20-30	>30	>30
<b>Doppler parameters (quantitative)</b>						
○ Regurgitant fraction (%)	<15	<15	15-30	30-40	40-50	>50

# Paravalvular Leak (S3HR and S3i)

**85% under GA  
with TEE**

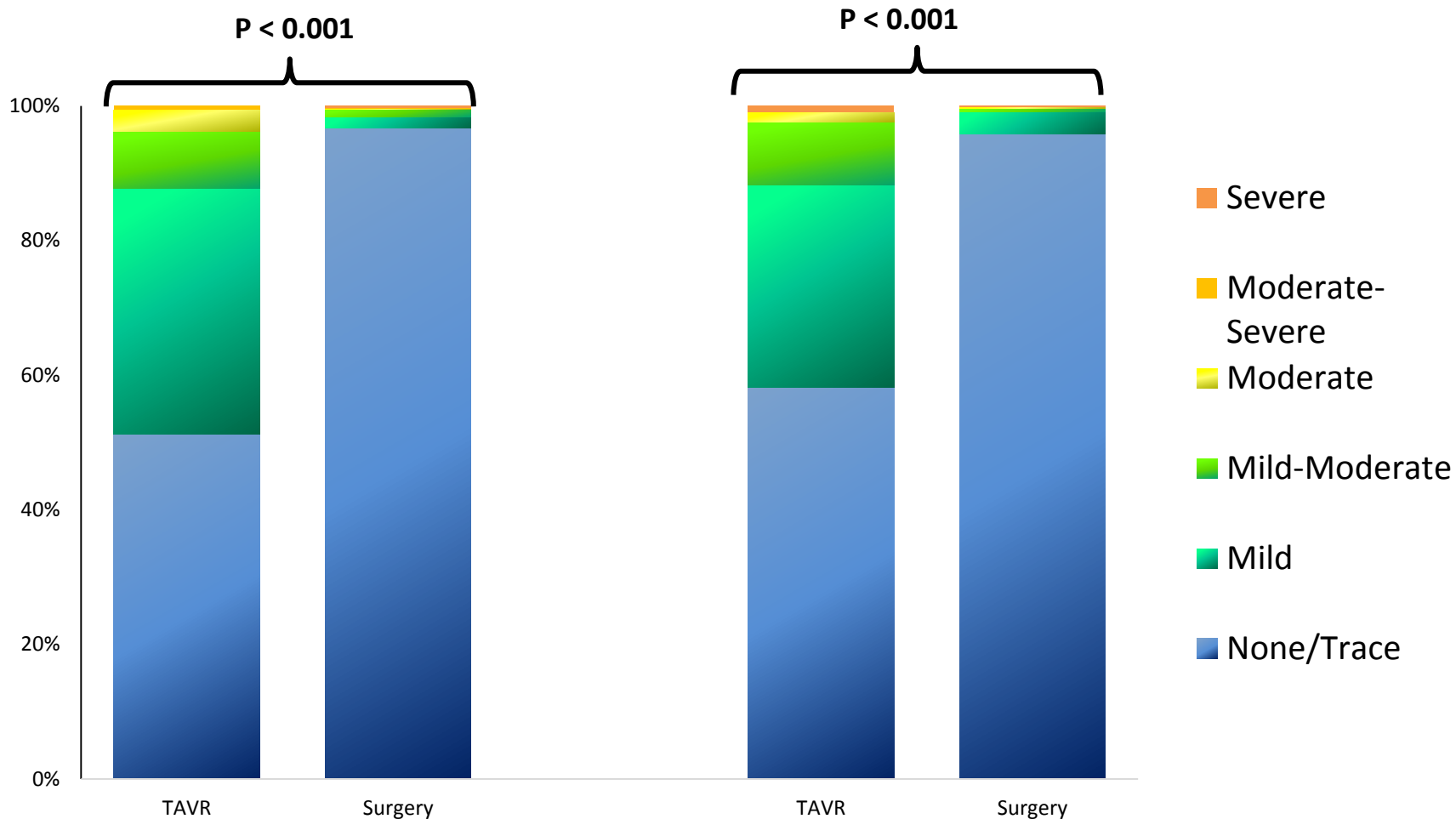


No. of Echos

1504

# S3i – Paravalvular Regurgitation

## 5-Class Grading Scheme

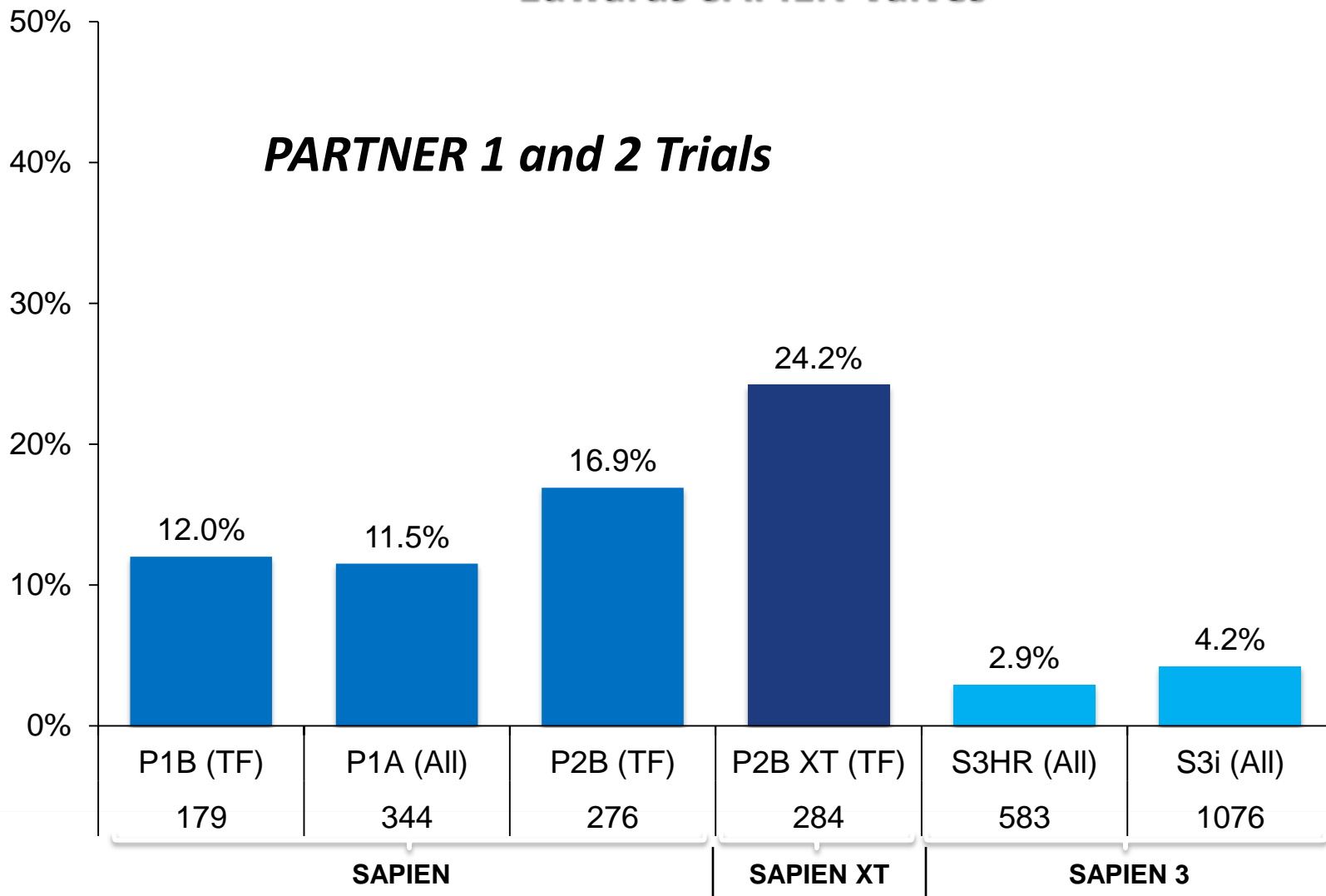


No. of echos	30 Days	2 Years
P2A Surgery	755	610
S3i TAVR	992	875

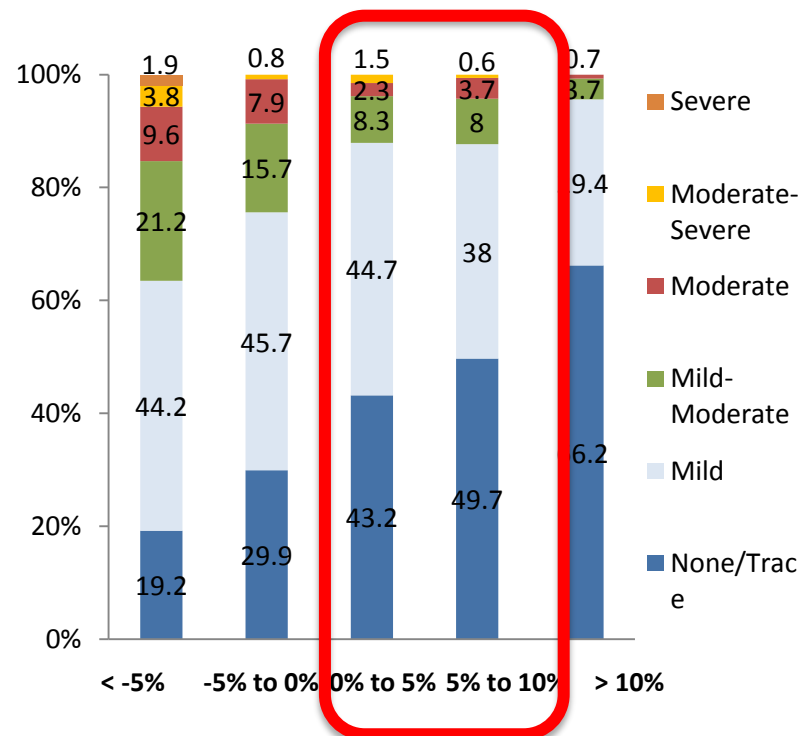
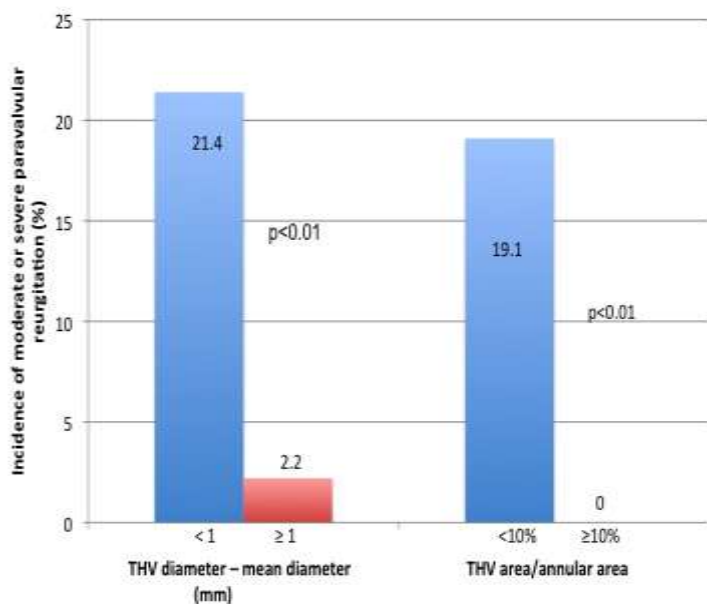
# Moderate/Severe PVL at 30 Days

## Edwards SAPIEN Valves

*PARTNER 1 and 2 Trials*



# Know your device characteristics



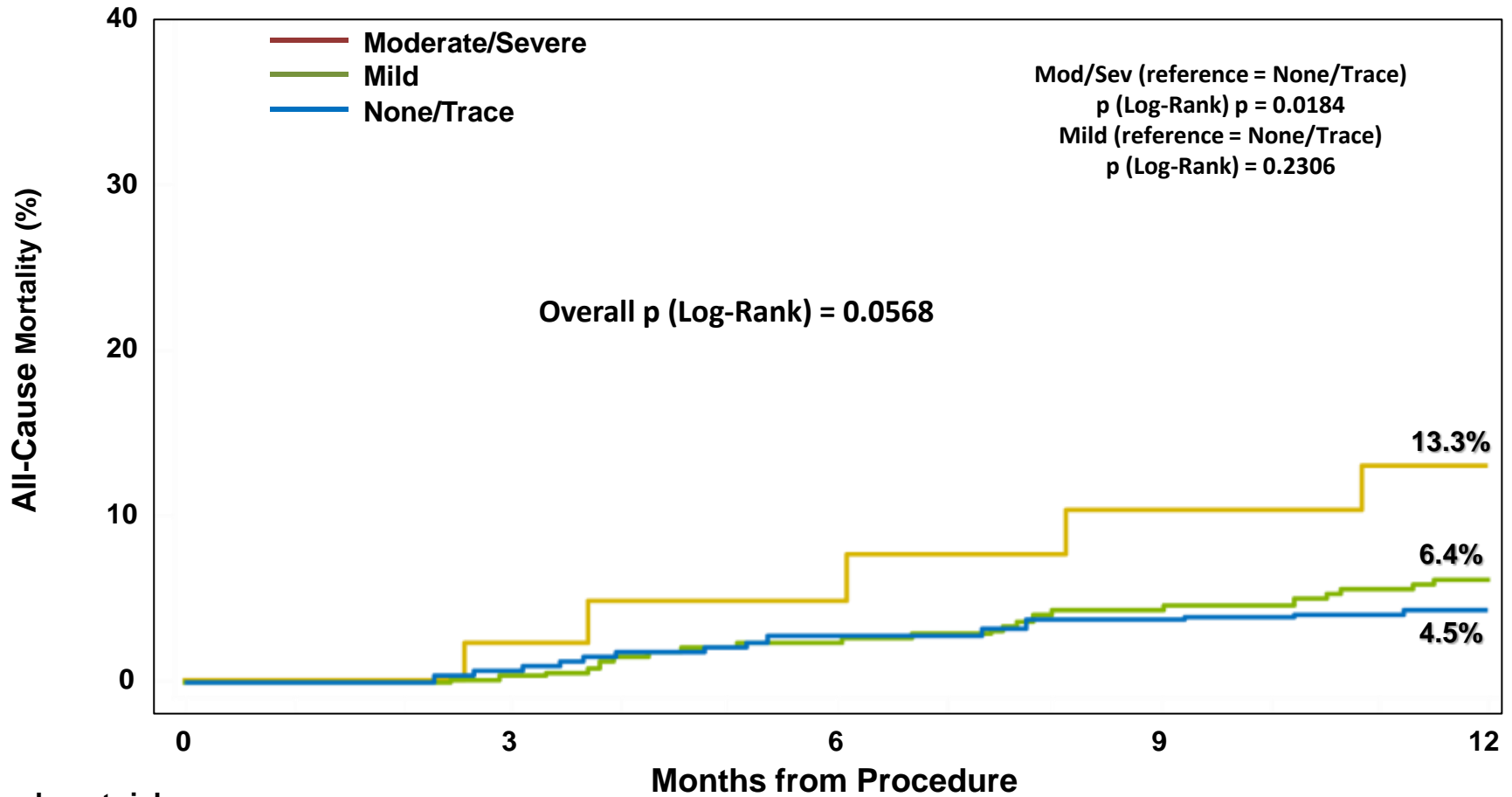
Willson et al. JACC April 3 2012

Blanke et al. EuroPCR 2015



# Mortality by PVR Severity

## S3i

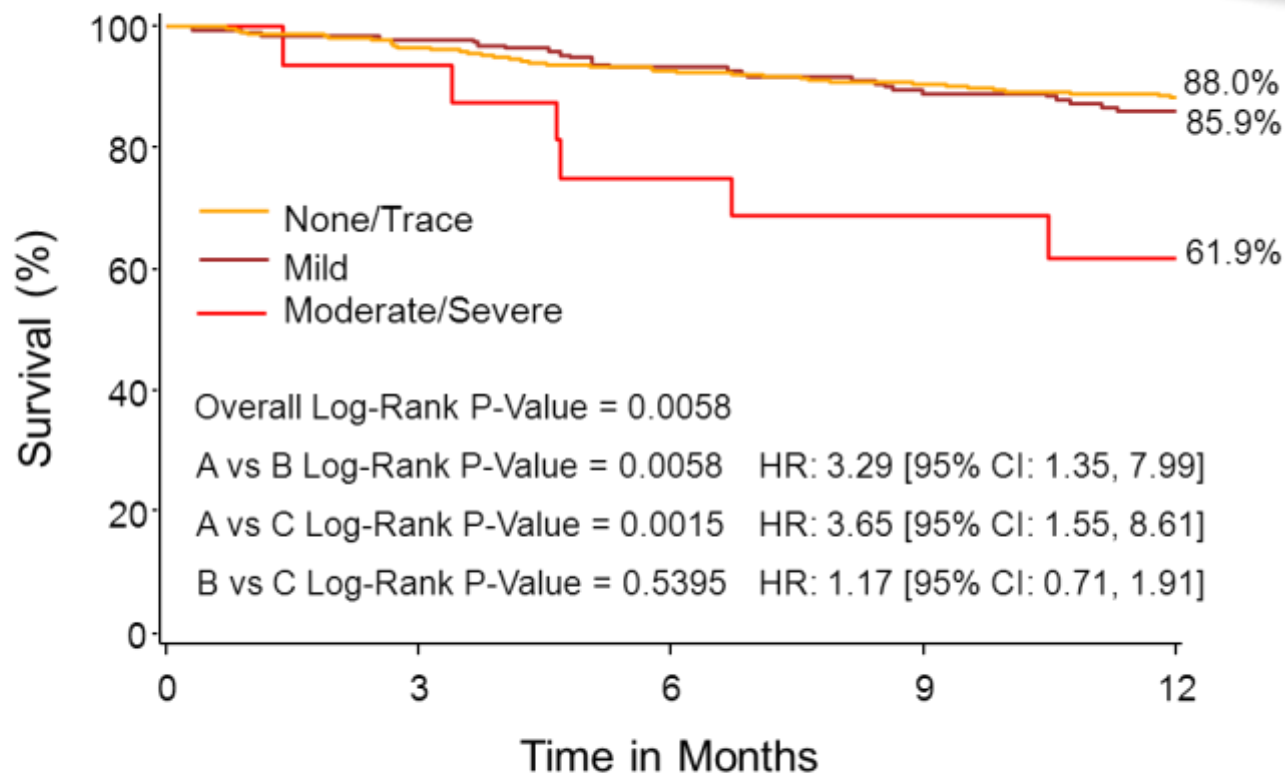


Number at risk:

Mod/Sev	38	37	36	33	31
Mild	446	440	430	419	406
None/Trace	508	503	492	484	474

# Impact of PVL on Mortality

## S3HR



### Number at risk:

	0	3	6	9	12
Moderate/Severe	16	15	12	11	9
Mild	191	186	177	168	110
None/Trace	351	339	321	309	219

# Conclusions

- Rates of moderate to severe PVR after TAVR are significantly lower than those seen with prior iterations of balloon expandable valves
- Device iteration as well as procedural technique are likely responsible for these improvements
- Mild PVR does not appear to have an impact on mortality at one year in either high risk or intermediate risk cohorts
- PVR assesment remains challenging and more granular grading schemes may help with consistency
- Further analyses using granular grading scale forthcoming