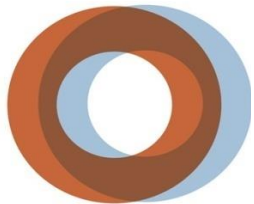


Paravalvular Regurgitation is a Risk Factor Following TAVI

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INSTITUT
UNIVERSITAIRE
DE CARDIOLOGIE
ET DE PNEUMOLOGIE
DE QUÉBEC



**Université
LAVAL**

Disclosure

Philippe Pibarot

Financial relationship with industry:

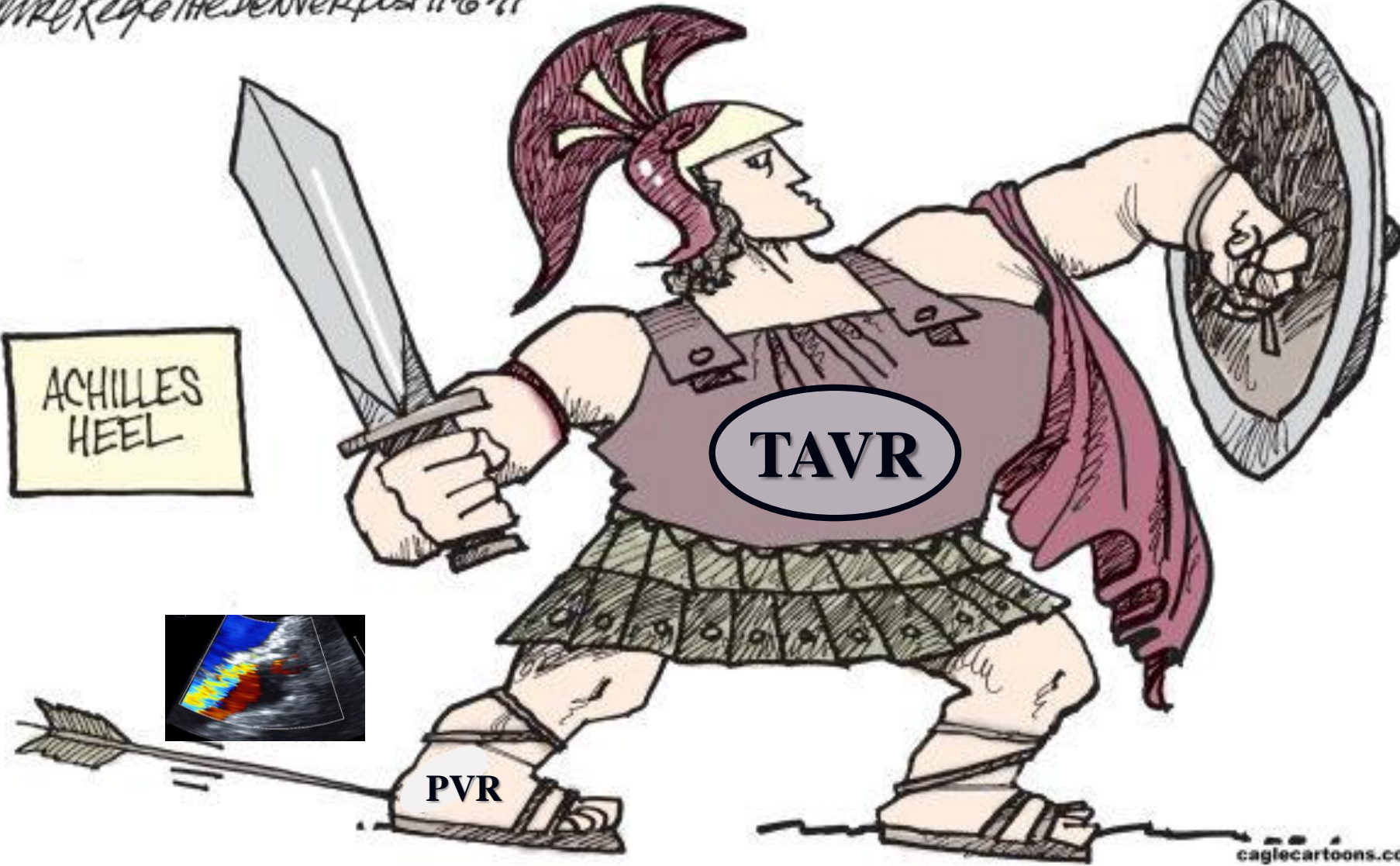
- **Edwards Lifesciences: Echo CoreLab for PARTNER II - SAPIEN 3 and TAVR-UNLOAD**
- **V-Wave: Echo CoreLab**
- **Cardiac Pheonix: Echo CoreLab**

Other financial disclosure:

- **Research Grants from Canadian Institutes of Health**
- **Research and Heart & Stroke Foundation of Quebec**

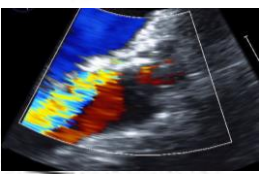
Off label Use: None

Mike Keefe THE DENVER POST 11-6-11



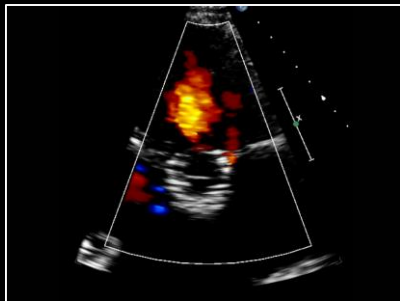
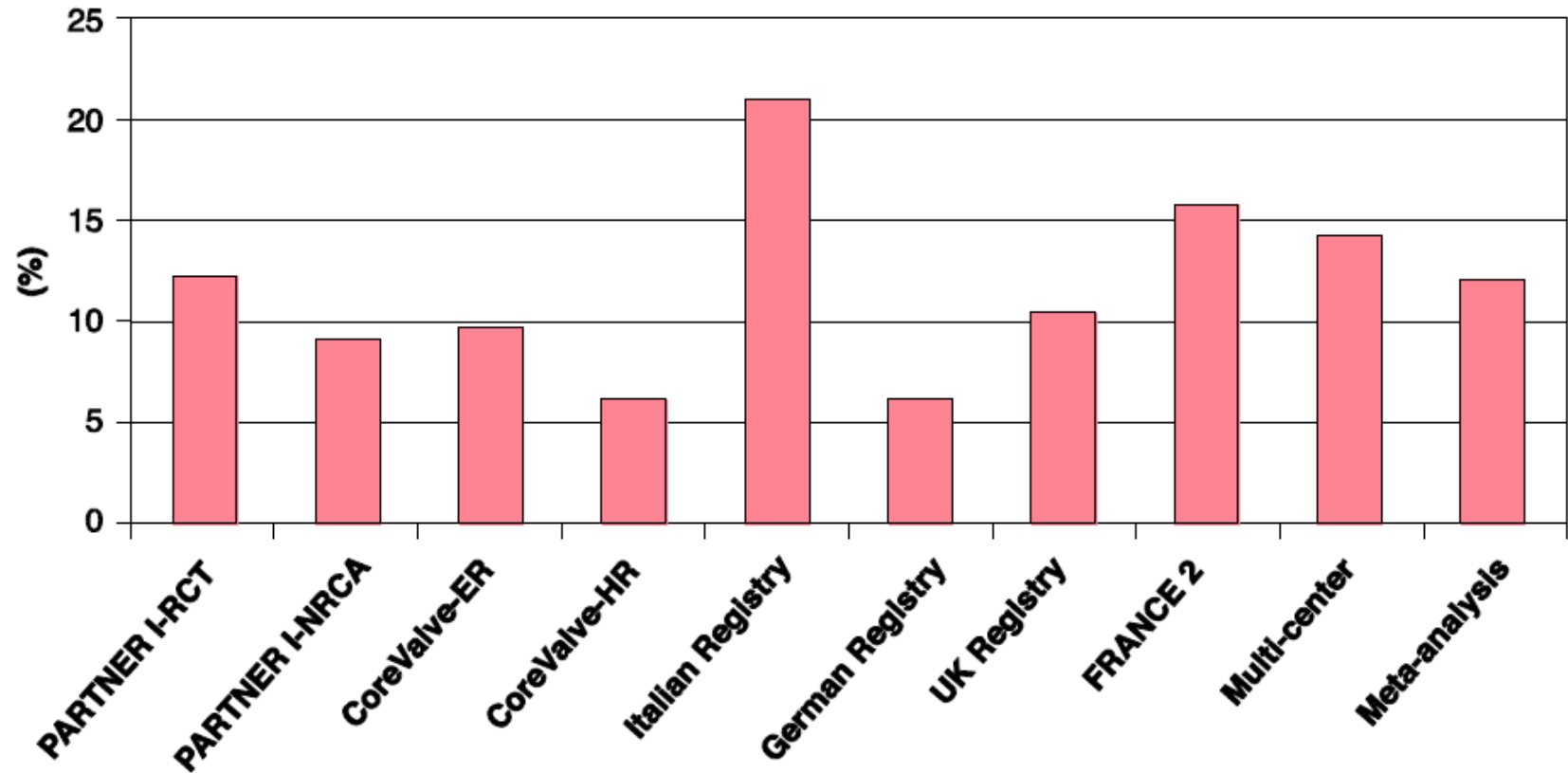
ACHILLES
HEEL

TAVR



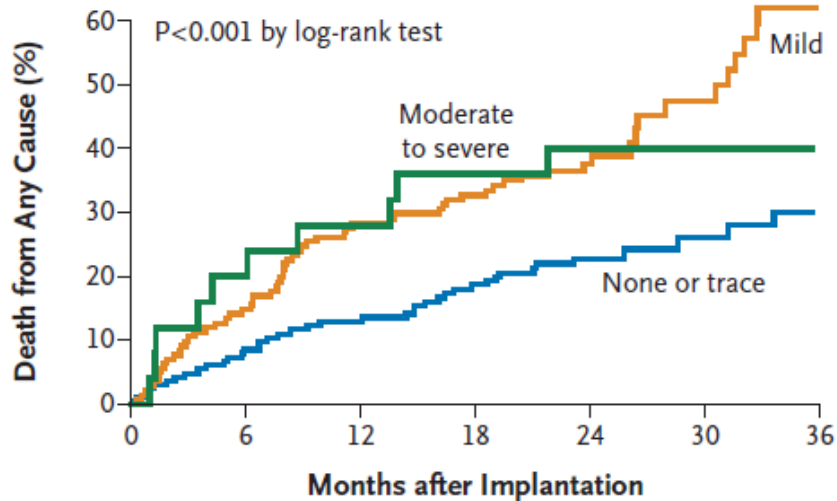
PVR

Incidence of Moderate/Severe PVR in TAVR



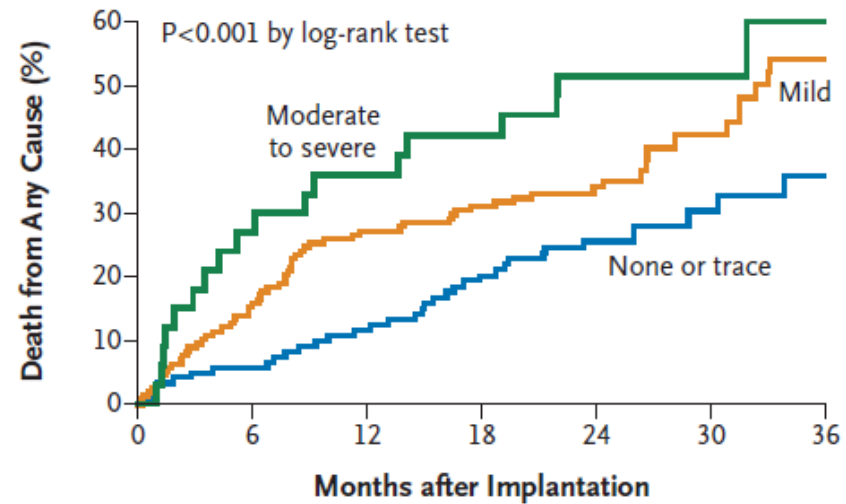
Impact of Paravalvular Regurgitation on 2-Year Outcomes: PARTNER-1 A Trial

Paravalvular Regurgitation



No. at Risk		0	6	12	18	24	30	36
None or trace	158	142	134	121	84	39	15	
Mild	136	115	95	86	51	21	10	
Moderate to severe	24	19	17	15	13	5	2	

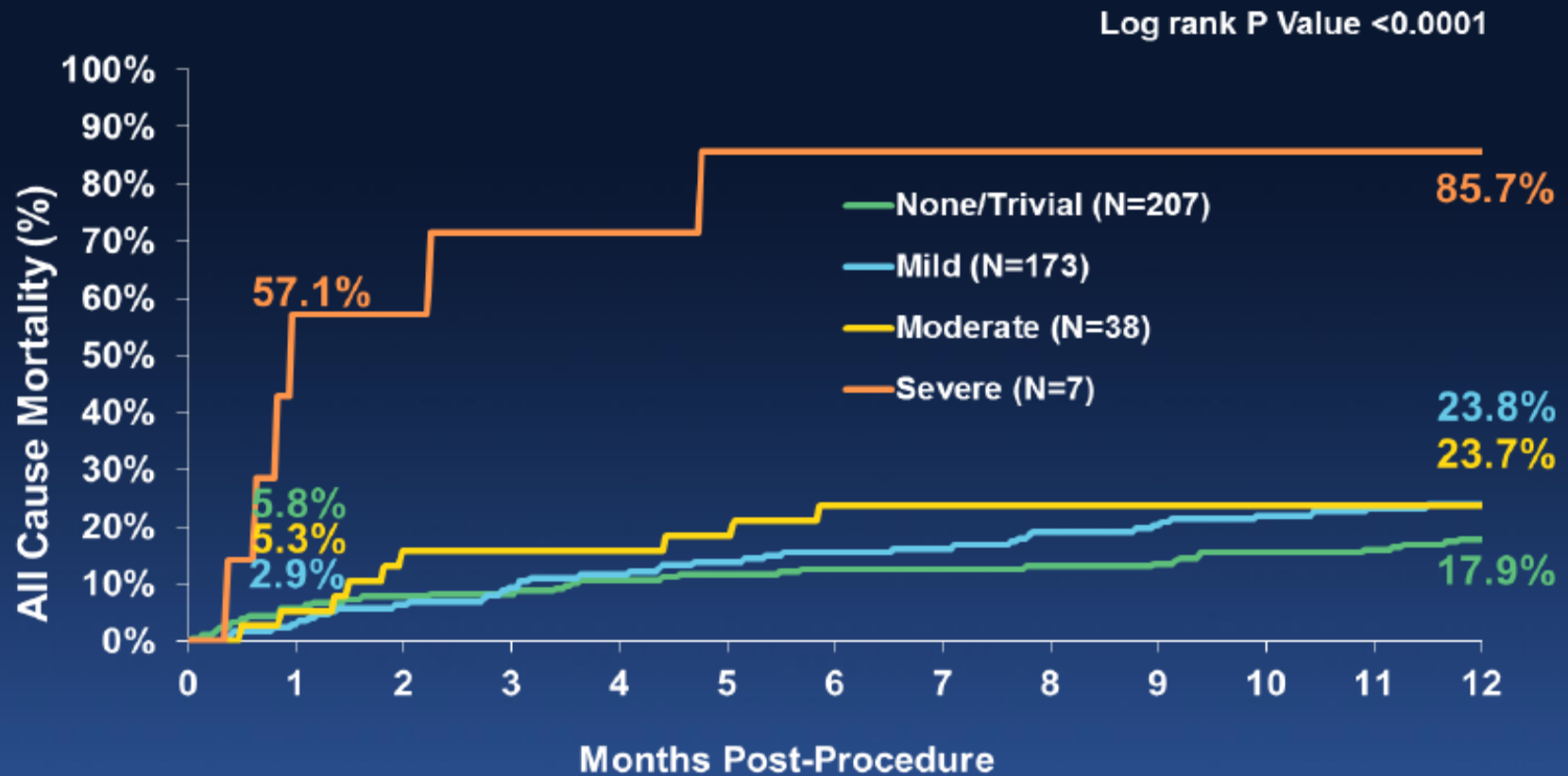
Total (Paravalvular+Central) Regurgitation



No. at Risk		0	6	12	18	24	30	36
None or trace	125	117	108	95	64	29	10	
Mild	162	136	118	109	70	31	15	
Moderate to severe	34	25	22	19	15	6	2	

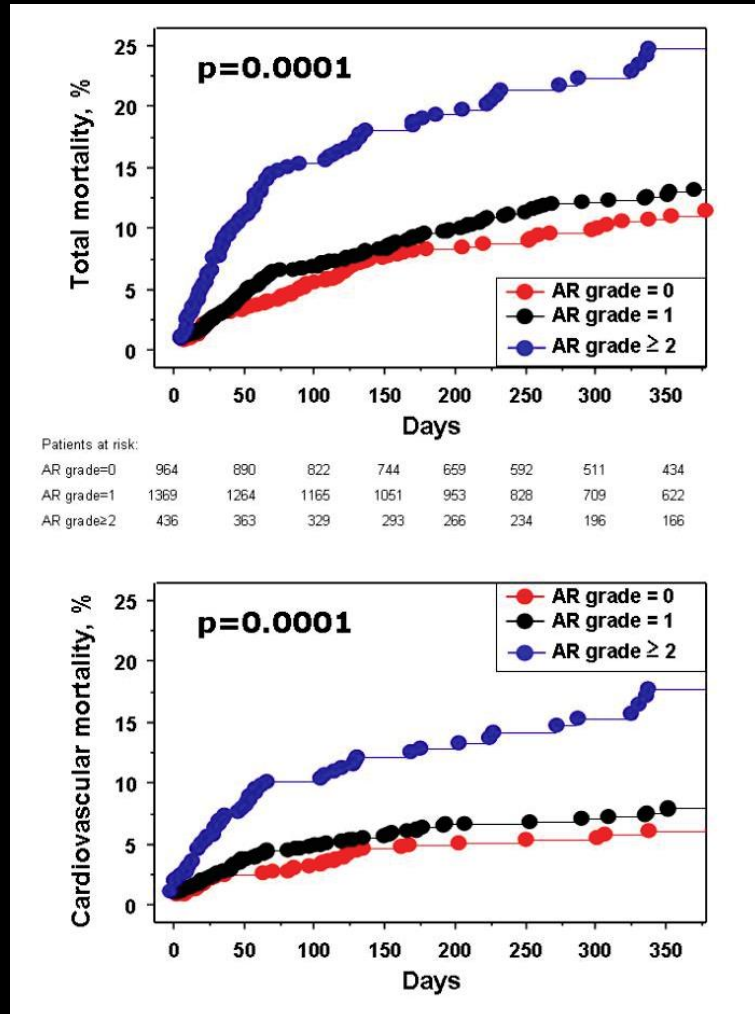
Impact of AR on Mortality

CoreValve Pivotal Trial

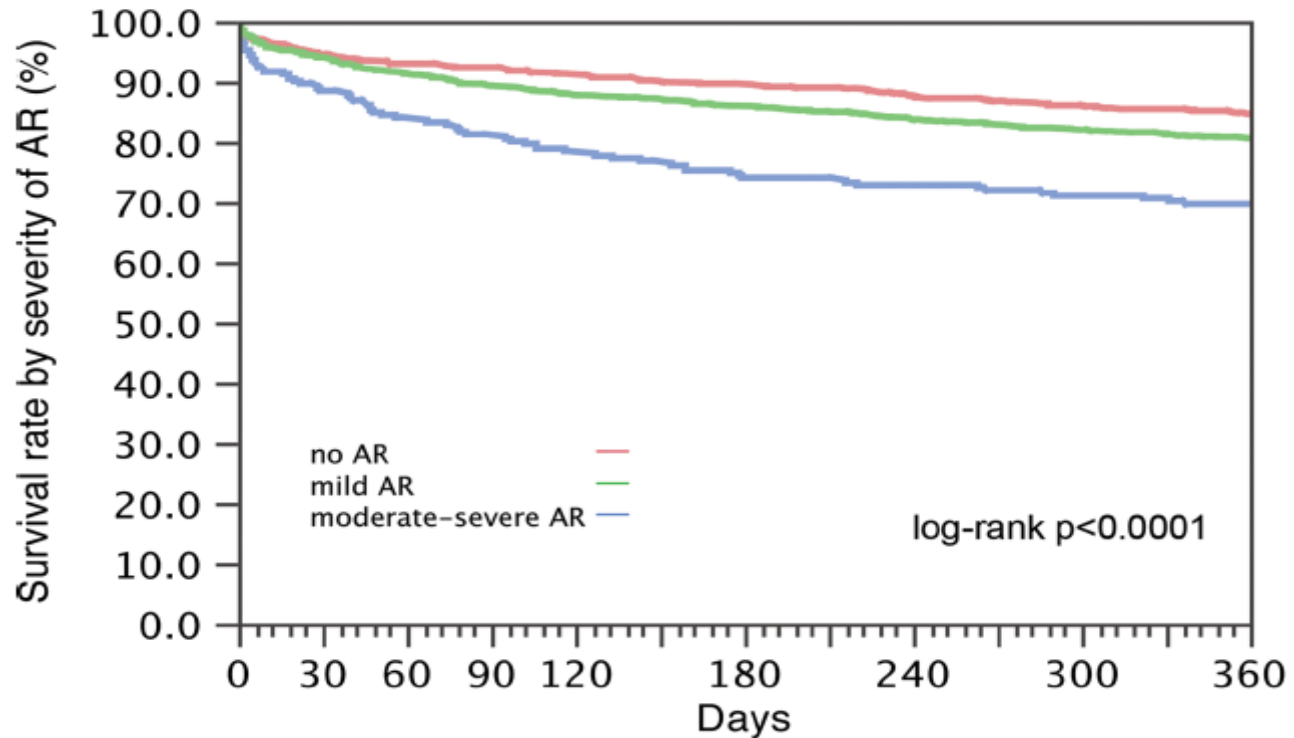


Impact of AR Post-TAVI / France-2 Registry

n= 2769



Impact AR Post-TAVI / UK Registry

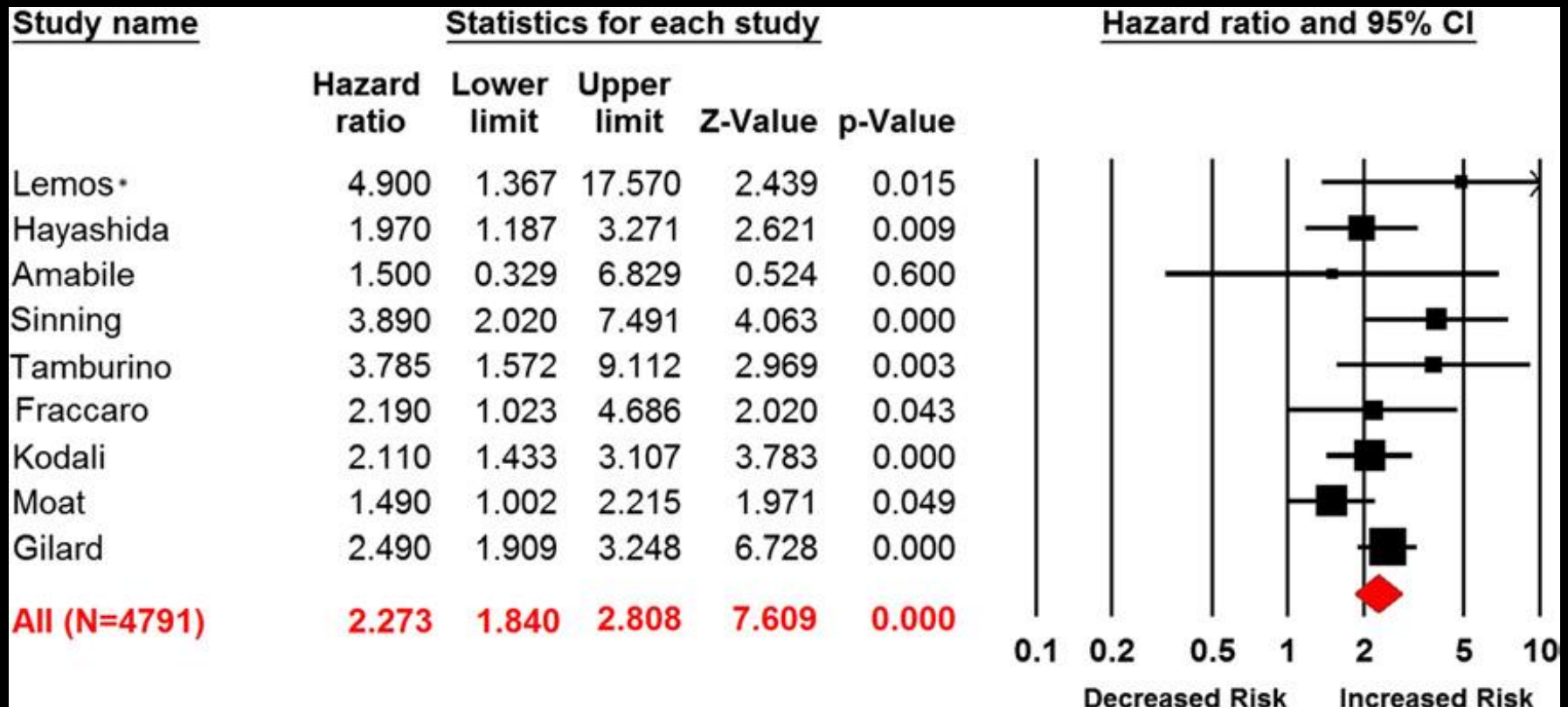


No at risk	Baseline	90 days	180 days	270 days	360 days
Total	2434	2150	2064	1795	1540
No AR	783	714	692	604	525
mild AR	1398	1233	1186	1026	874
moderate-severe AR	253	203	186	165	141

Impact of Moderate / Severe Aortic Regurgitation After TAVI

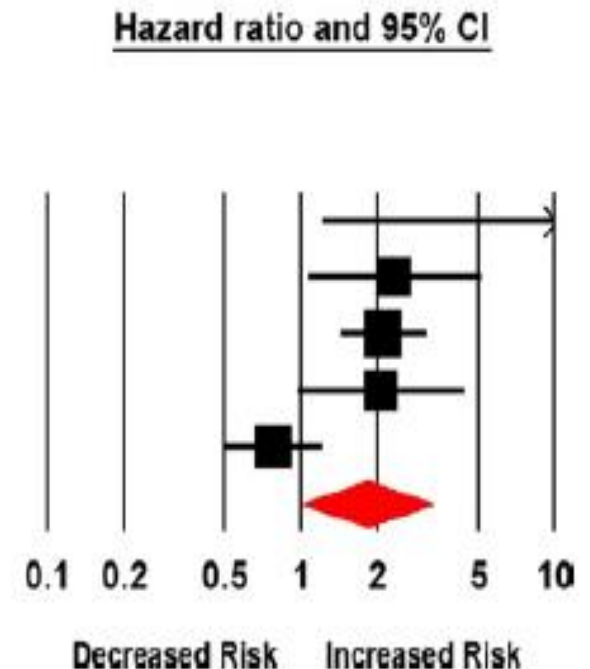
Meta-Analysis and Systematic Review of Literature

Impact of Moderate-Severe AR on Mortality

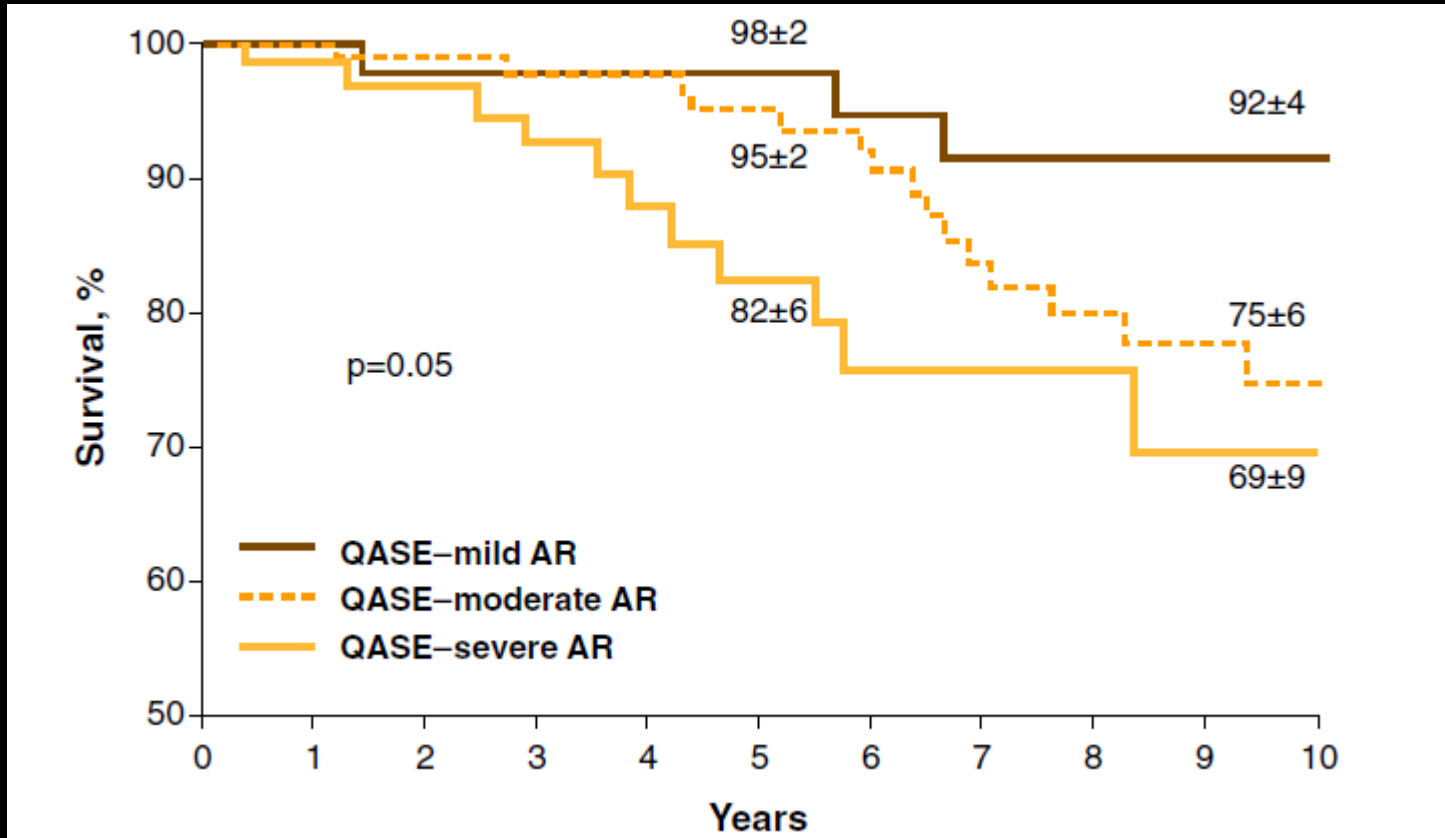


Impact of Mild AR on Mortality after TAVI: A Meta-analysis

<u>Study name</u>	<u>Statistics for each study</u>				
	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
All (N=1620)	1.829	1.005	3.329	1.975	0.048



Survival Under Conservative Management After Diagnosis of Native AR

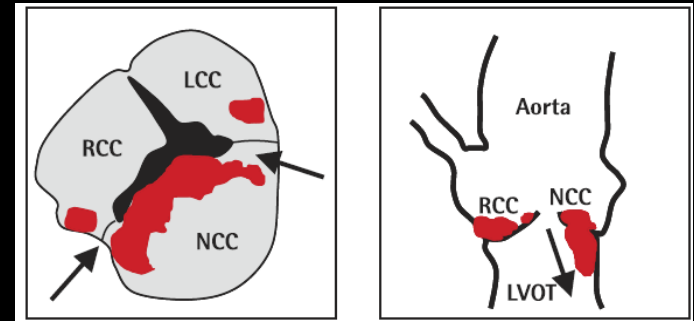


Potential explanations for the Association between Mild PVR and mortality following TAVI

- **Patients with mild PVR have worse baseline risk profile compared to none/trace PVR**
- **Severity of PVR is underestimated**
- **Some subsets of patients with severe AS may be more vulnerable to AR**

Predictors of Paravalvular Regurgitation following TAVI

- **Male gender**
- **NYHA Class IV**
- **Atrial fibrillation**
- **AR at baseline**
- **MR at baseline**
- **More severe and asymmetric valve calcification**
- **Larger aortic annulus**
- **Smaller cover index**
- **Inadequate valve positioning**
- **Self expanding valve**



Sinning et al. JACC, 2012
Haensig M, EJCTS, 2012
Ewe et al. Am J Cardiol 2011
Uebeaum et al. JACC, 2012
Sinning et al. JACC 2013

Baseline Characteristics of TAVR Patients with Paravalvular Regurgitation in the PARTNER Trial

Table 2 Baseline echocardiographic characteristics of patients by severity of paravalvular regurgitation

Baseline parameters	Severity of paravalvular regurgitation			P-value (all groups) ^a
	(a) None/trace (n = 1288)	(b) Mild (n = 925)	(c) Moderate/severe (n = 221)	
LVEDD (cm)	4.41 ± 0.74	4.60 ± 0.77	4.68 ± 0.74	<0.0001
LVESD (cm)	3.20 ± 0.92	3.35 ± 0.94	3.51 ± 0.92	<0.0001
Stroke volume (cc)	64.2 ± 19.6	68.5 ± 21.4	67.6 ± 25.0	0.01
Cardiac output	4.38 ± 1.41	4.62 ± 1.54	4.57 ± 1.59	0.08
LV EF (%)	53.7 ± 12.4	51.4 ± 13.2	50.2 ± 13.9	<0.0001
LV mass (g)	238.7 ± 74.1	260.3 ± 78.3	267.2 ± 73.6	<0.0001
LVOT diameter (cm)	1.98 ± 0.18	2.04 ± 0.18	2.06 ± 0.19	<0.0001
Annulus diameter (cm)	21.27 ± 1.86	21.64 ± 1.83	21.91 ± 1.88	<0.001
EOA (cm ²)	0.65 ± 0.19	0.66 ± 0.19	0.65 ± 0.19	0.25
Aortic regurgitation				
None/trace	44.7%	42.8%	34.2%	0.02
Mild	46.5%	46.8%	41.2%	0.36
Moderate/severe	8.6%	10.3%	24.4%	<0.0001
Mitral regurgitation				
None/trace	29.9%	25.8%	17.8%	0.001
Mild	50.7%	51.7%	46.1%	0.37
Moderate/severe	19.5%	22.5%	36.1%	<0.0001

Impact of PVR on Mortality in the PARTNER Trial

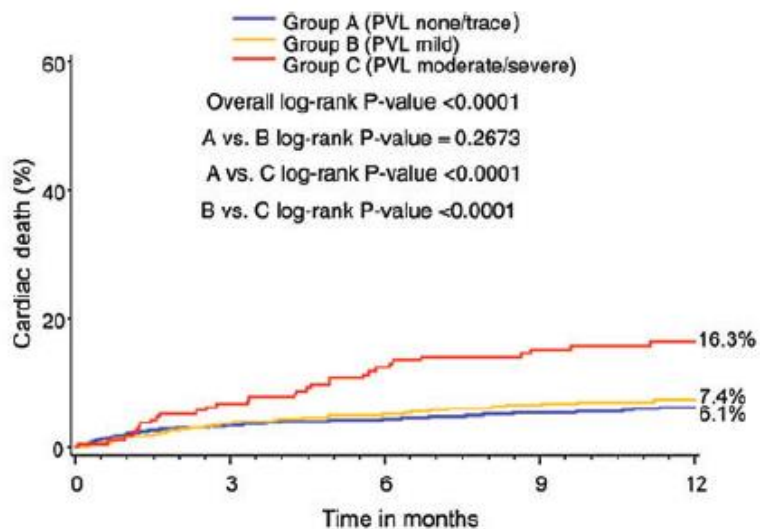
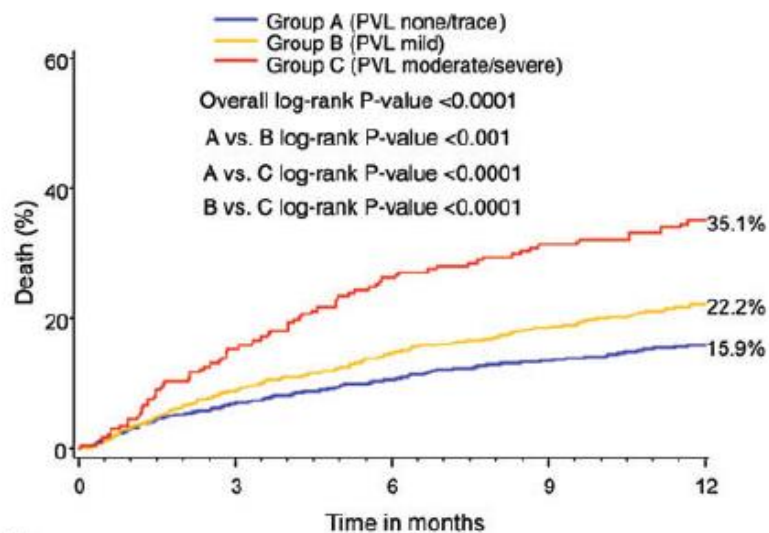


Table 4 Multivariable predictors of all-cause 1-year mortality

Multivariable analysis: baseline and procedural predictors of 1-year mortality

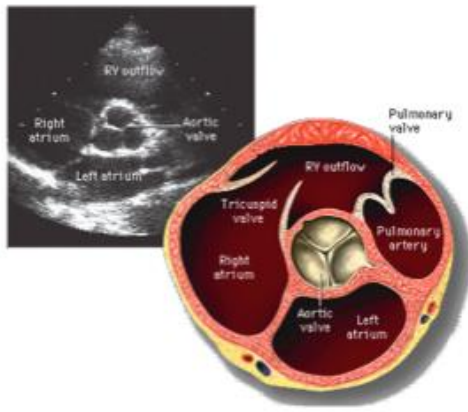
Variable	Hazard ratio	95% Confidence interval	P-value ^a
Major arrhythmia	1.41	1.14–1.75	0.002
TF vs. TA	0.73	0.59–0.91	0.005
AV annulus diameter (per 1 mm increase)	1.07	1.03–1.11	0.001
BMI (per 1 kg/m ² increase)	0.95	0.93–0.97	<0.0001
Total distance walked (per 10 m increase)	0.97	0.96–0.98	<0.0001
AV mean gradient (per 1 mmHg)	0.98	0.97–0.99	<0.0001
Paravalvular regurgitation			
None/trace	Referent	–	–
Mild	1.35	1.07–1.72	0.013
Moderate/severe	2.20	1.60–3.03	<0.0001
Renal disease (CR ≥2)	1.35	1.04–1.74	0.023

Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document[†]

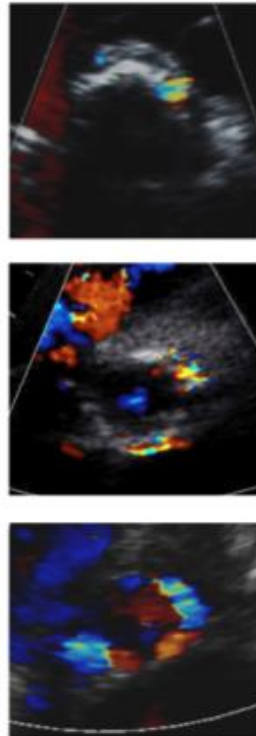
	Prosthetic aortic valve regurgitation		
	Mild	Moderate	Severe
Semi-quantitative parameters			
Diastolic flow reversal in the descending aorta—PW	Absent or brief early diastolic	Intermediate	Prominent, holodiastolic
Circumferential extent of prosthetic valve paravalvular regurgitation (%) ^h	< 10%	10–29%	≥ 30%
Quantitative parameters ^c			
Regurgitant volume (mL/beat)	< 30 mL	30–59 mL	≥ 60 mL
Regurgitant fraction (%)	< 30%	30–49%	≥ 50%
EROA (cm ²)	0.10 cm ²	0.10–0.29 cm ²	≥ 0.30 cm ²

Grading Severity of Paravalvular Regurgitation

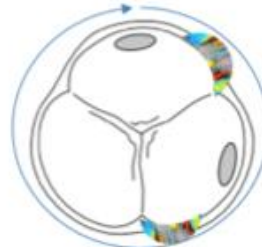
A



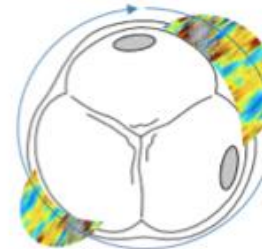
B



Circumference = 6"
 AR = $0.1 + 0.35 = 0.45$ "
 Ratio = 8%
 Severity = Mild



Circumference = 6"
 AR = $0.5 + 0.5 = 1.0$ "
 Ratio = 17%
 Severity = Moderate
 (Trans AR also present)

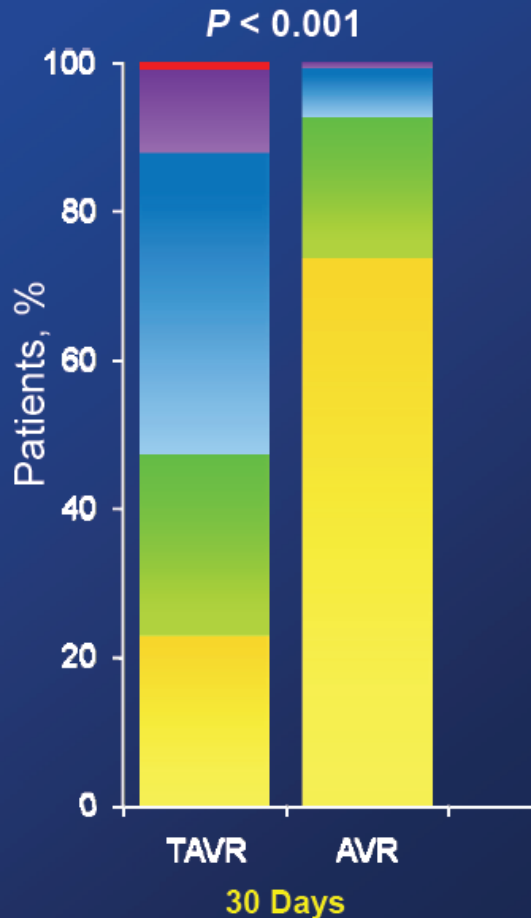


Circumference = 6"
 AR = $0.6 + 1.1 = 1.7$ "
 Ratio = 28%
 Severity = Severe

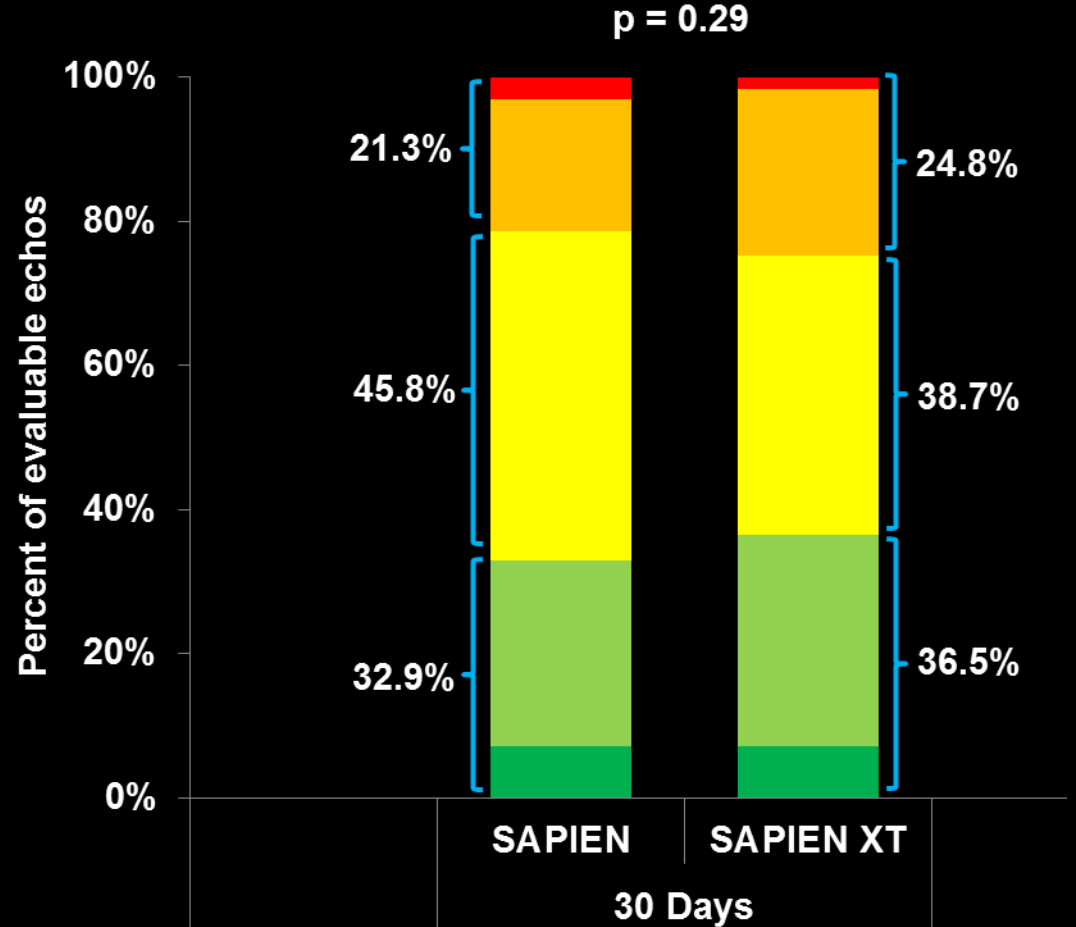
Total Aortic Regurgitation PARTNER I versus PARTNER II-B



PARTNER-IA



PARTNER-II-B



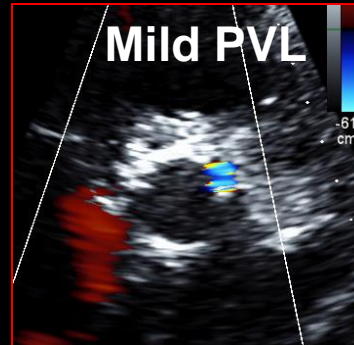
None Trace Mild Moderate Severe

None Trace Mild Moderate Severe

Grading of Paravalvular Regurgitation by Circumferential Extent of the Jet

ASE Guidelines & PARTNER II Trial:

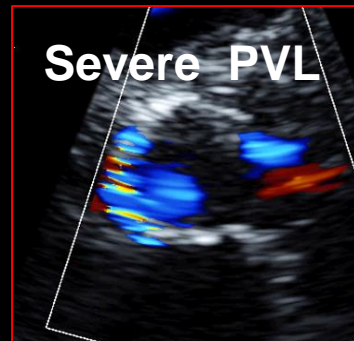
Mild PVL
<10% of the sewing ring



Moderate PVL
10-20% of the sewing ring



Severe PVL
>20% of the sewing ring



VARC 2 & PARTNER I Trial:

Mild PVL
<10% of the sewing ring

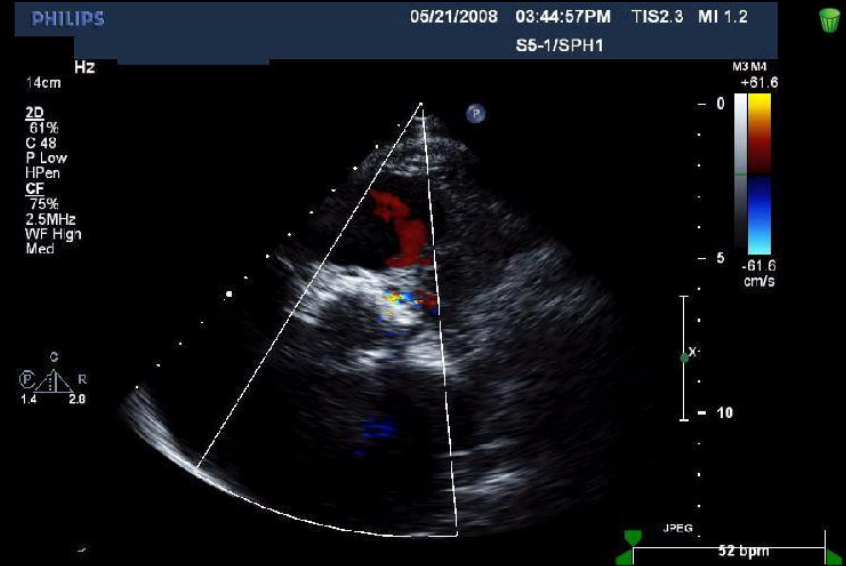
Moderate PVL
10-30% of the sewing ring

Severe PVL
>30% of the sewing ring

Douglas PS et al. J Am Soc
Echocardiography 2013;26(4): 348-358

Zoghbi WA et al. J Am Soc
Echocardiography 2009;22(9):975-1014

Multi-window Imaging is Key!

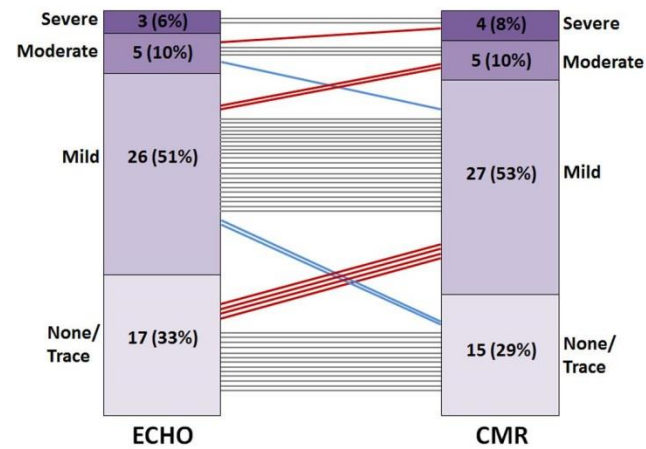


3-CLASS GRADING SCHEME	TRACE	MILD		MODERATE		SEVERE
4-CLASS GRADING SCHEME	1	1	2	2	3	4
UNIFYING 5-CLASS GRADING SCHEME	TRACE	MILD	MILD-TO-MODERATE	MODERATE	MODERATE-TO-SEVERE	SEVERE
Structural Parameters						
• Valve stent	Usually normal	Usually normal	Normal/abnormal	Normal/abnormal	Usually abnormal	Usually abnormal†
Doppler parameters (qualitative or semi-quantitative)						
• 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	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
Doppler parameters (quantitative)						
○ Regurgitant fraction (%)	<15	<15	15-30	30-40	40-50	>50

Multi-View/Multi Parametric TTE versus CMR to Assess AR Following TAVR

PRE

A

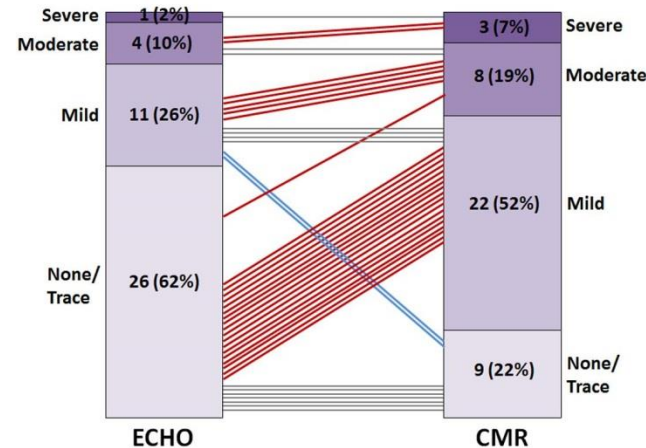


B

ECHO \ CMR	None/Trace	Mild	Moderate	Severe	Total
None/Trace	13 (76)	2 (8)	-	-	15
Mild	4 (24)	22 (84)	1 (20)	-	27
Moderate	-	2 (8)	3 (60)	-	5
Severe	-	-	1 (20)	2 (100)	3
Total	17	26	5	2	40/50 (80)

POST

C

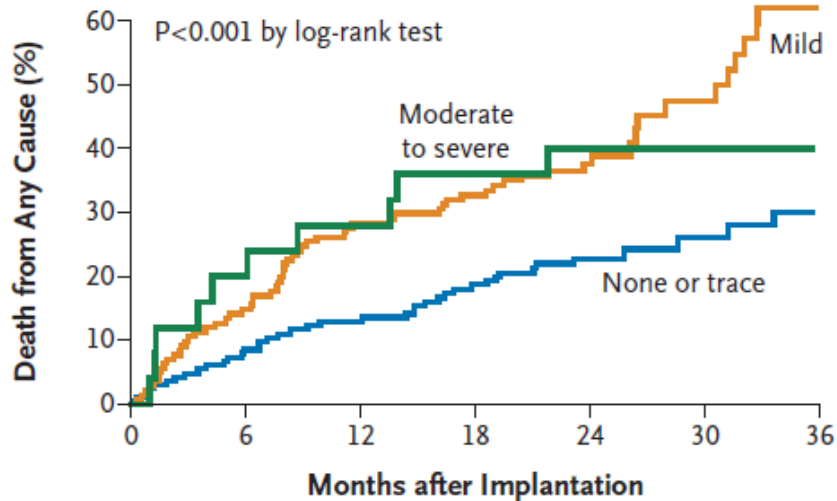


D

ECHO \ CMR	None/Trace	Mild	Moderate	Severe	Total
None/Trace	7 (27)	2 (18)	-	-	9
Mild	18 (69)	4 (36)	-	-	22
Moderate	1 (4)	5 (46)	2 (50)	-	8
Severe	-	-	2 (50)	1 (100)	3
Total	26	11	4	1	14/42 (33)

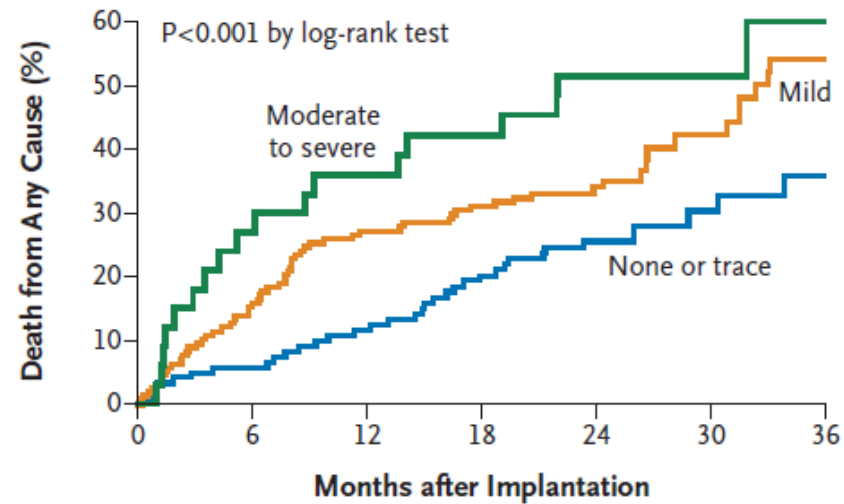
Impact of Paravalvular Regurgitation on 2-Year Outcomes: PARTNER-1 A Trial

Paravalvular Regurgitation



No. at Risk		0	6	12	18	24	30	36
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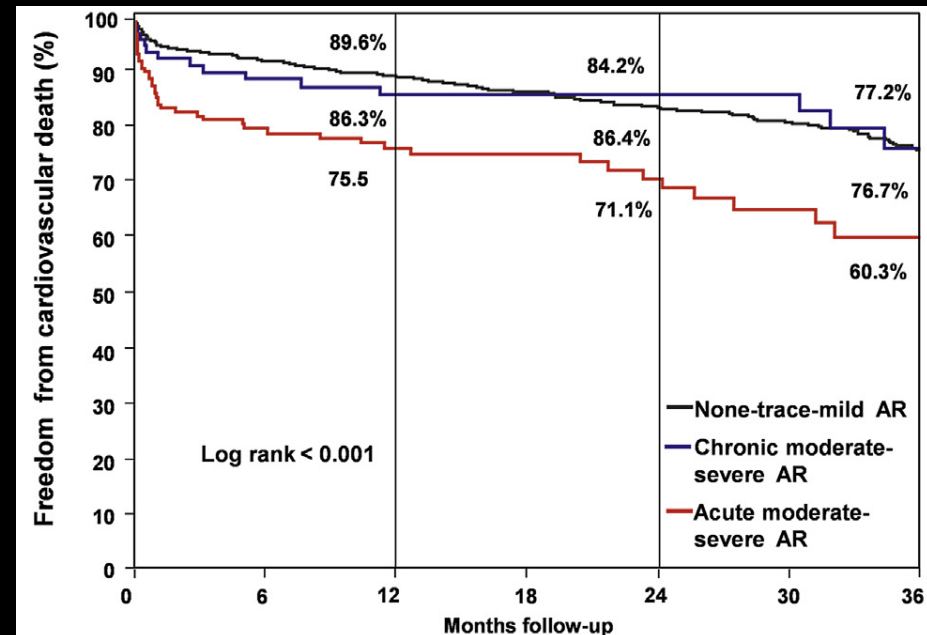
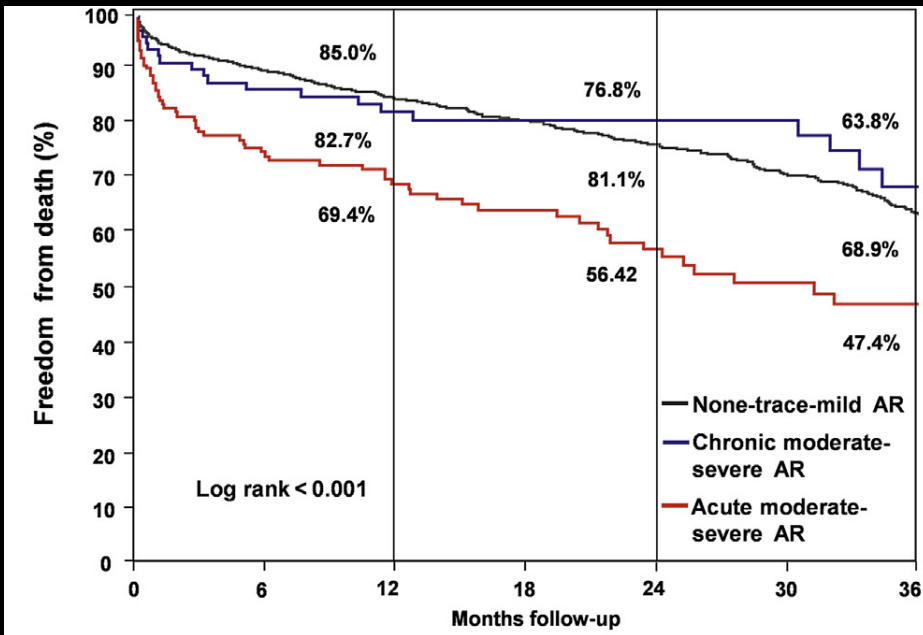
Total (Paravalvular+Central) Regurgitation



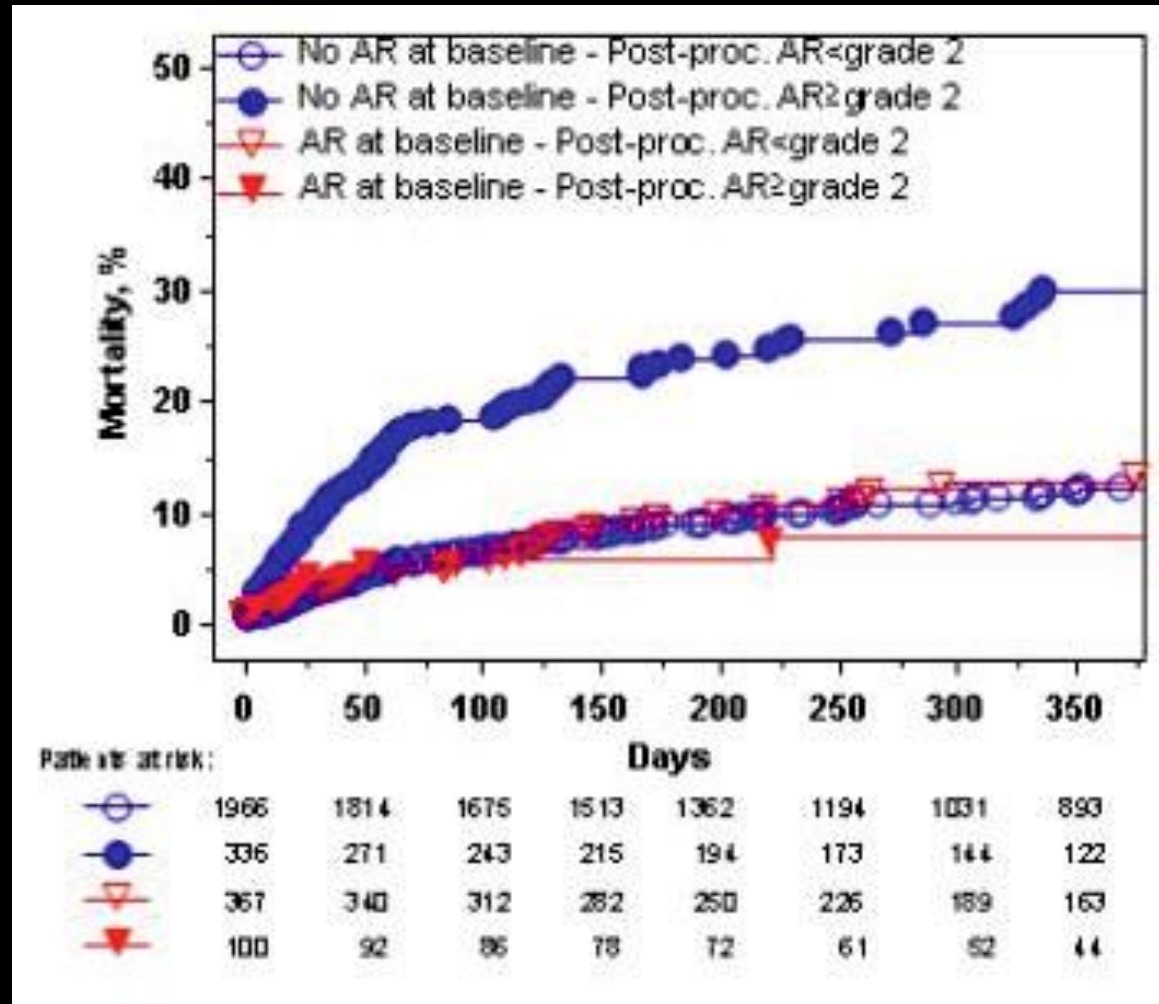
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Effect of Acuteness of AR on Mortality After TAVI:

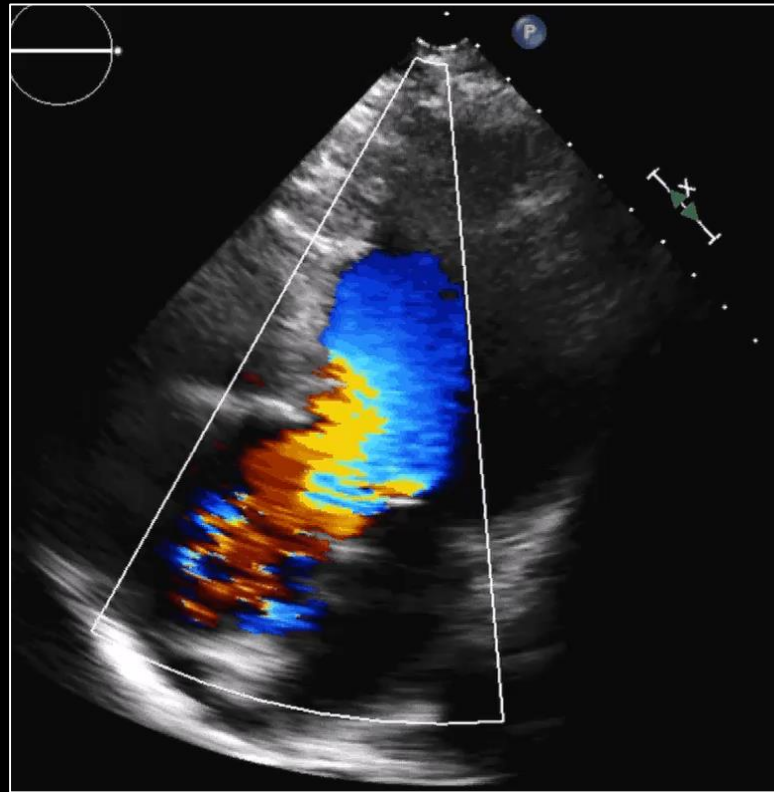
Multicenter Study (1735 Patients)



Effect of Acuteness of AR on Mortality After TAVI: France 2 Registry



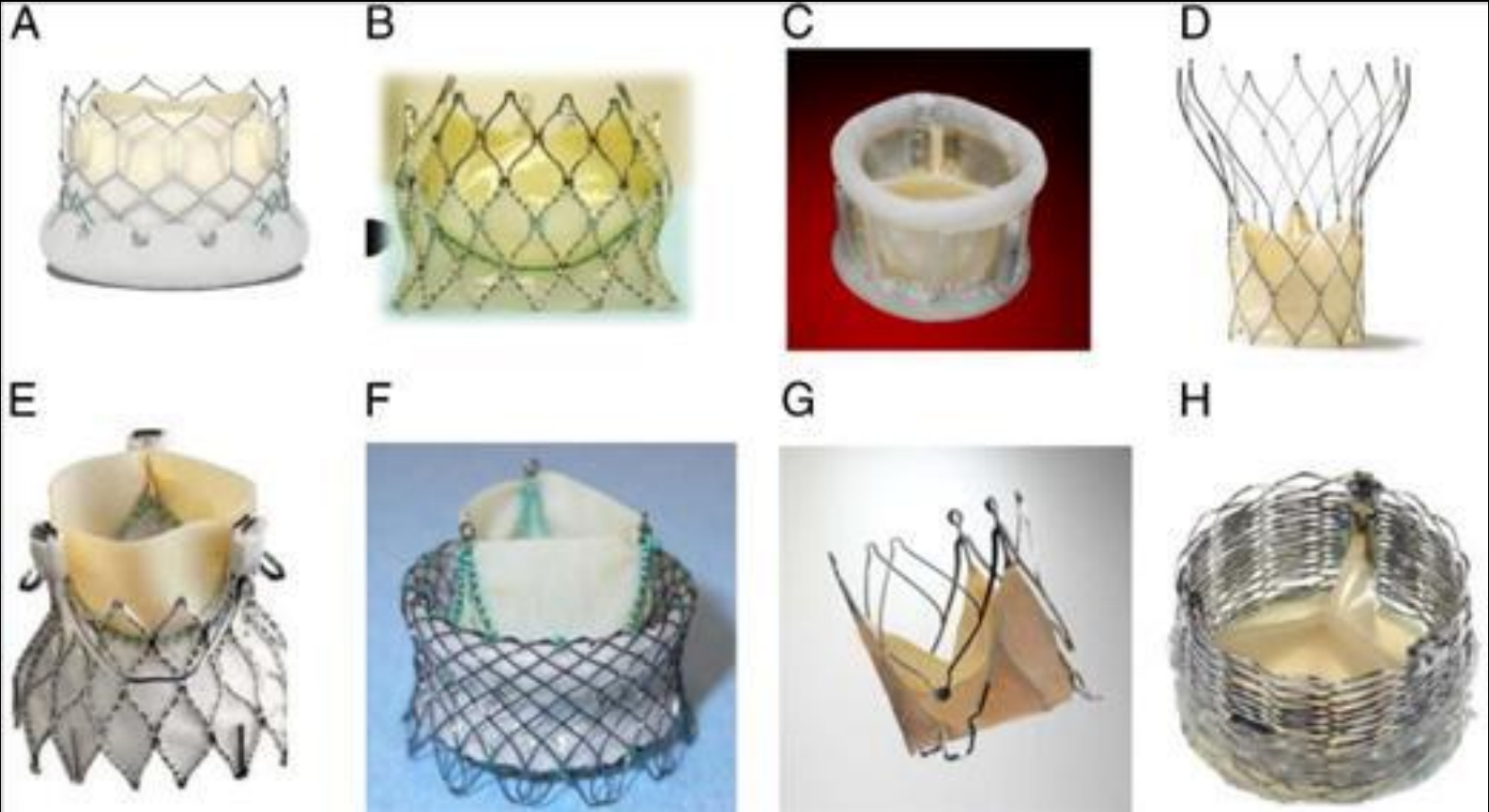
A moderate PVR may be well tolerated by a patient with pre-existing native AR



A mild PVR could be harmful in patients with pure AS

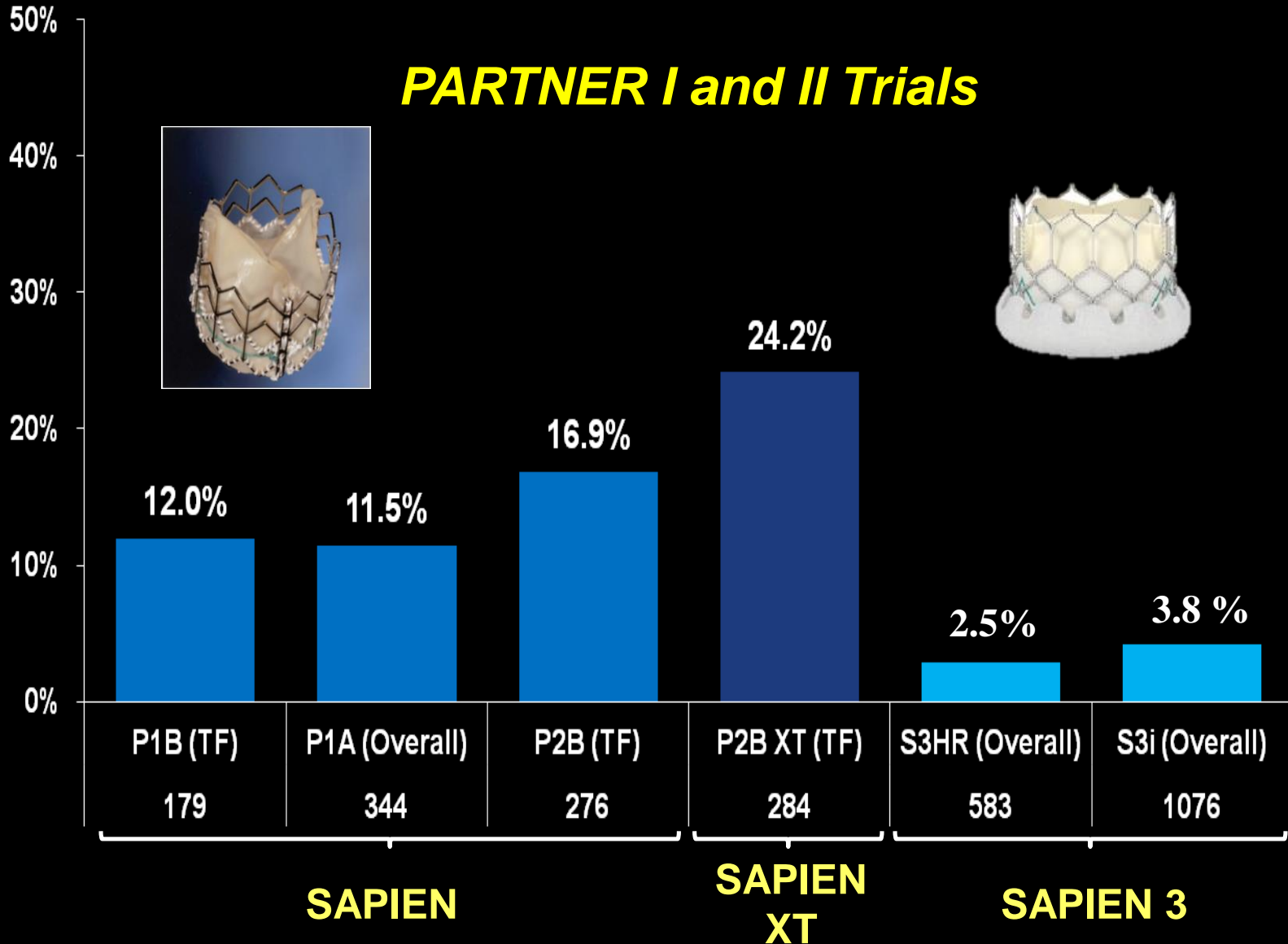


New Transcatheter Heart Valves to Prevent PVR

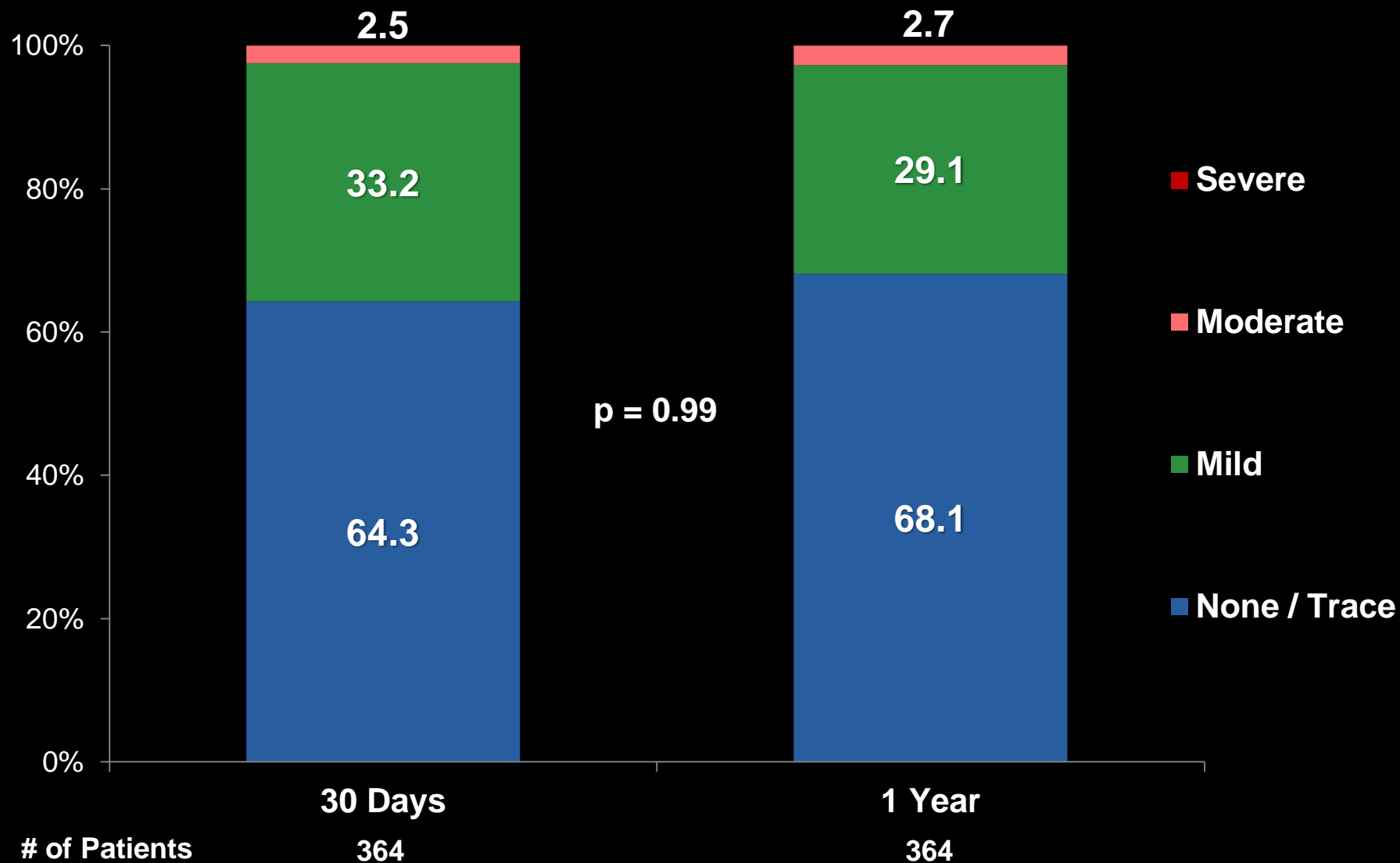


Moderate/Severe PVR at 30 Days

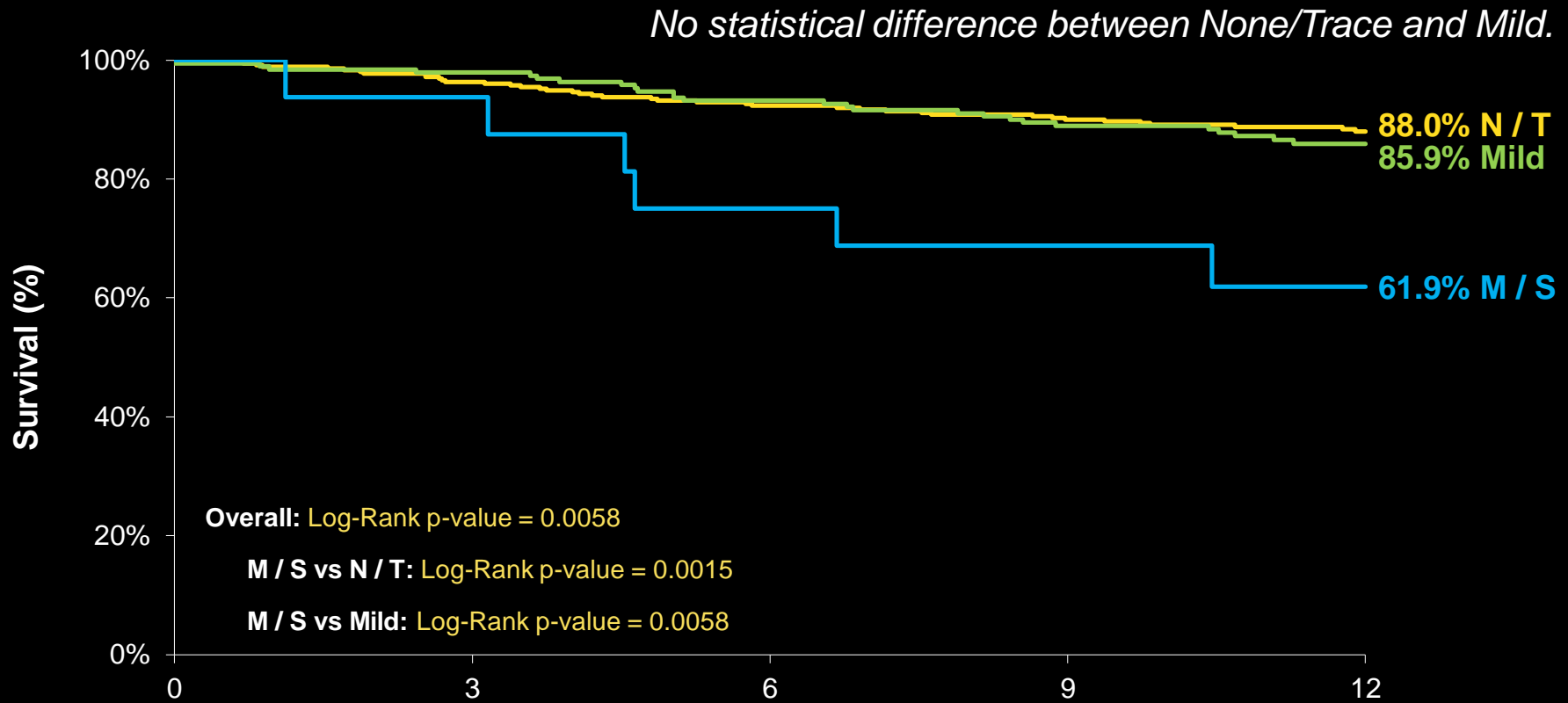
Edwards SAPIEN Valves



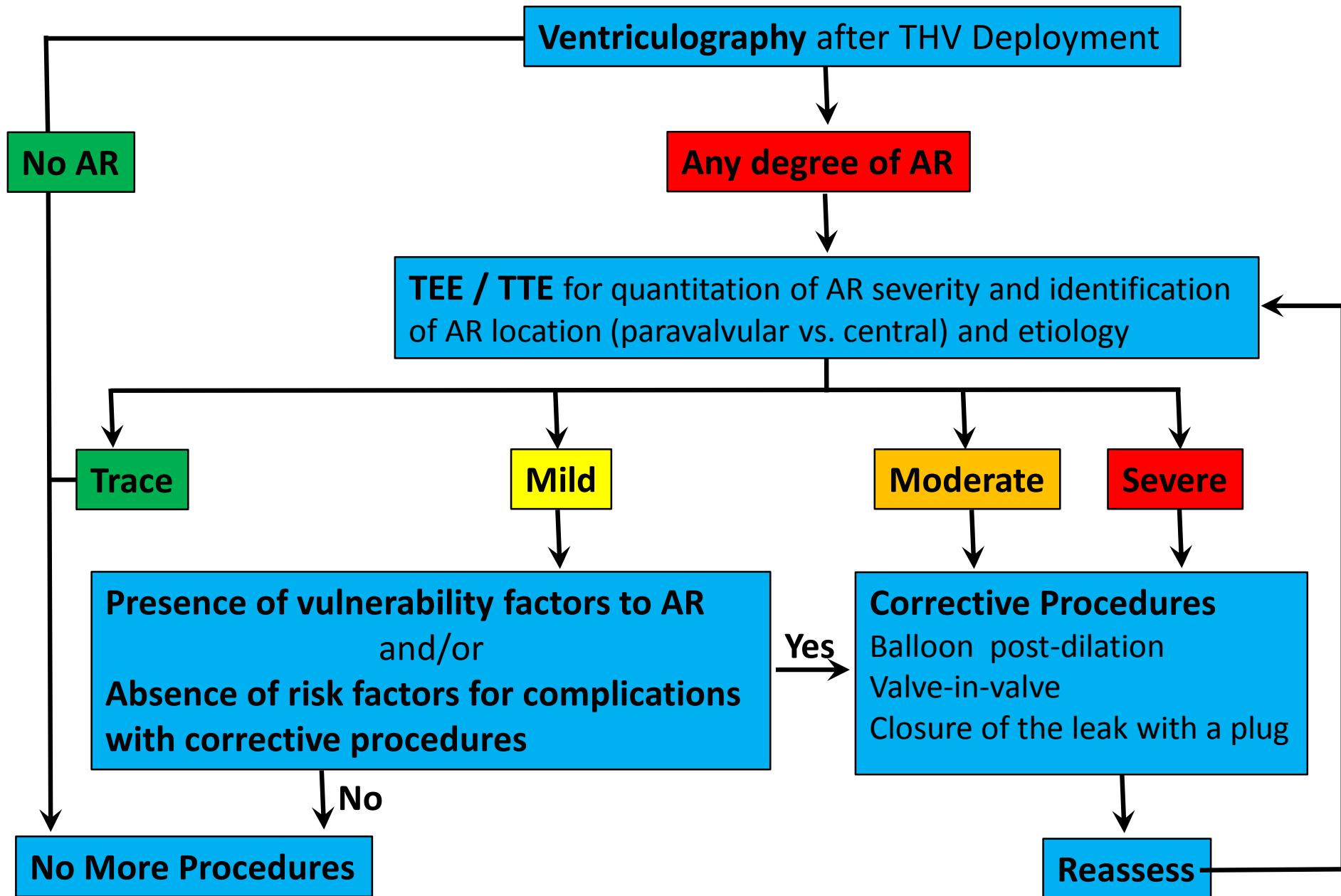
Paravalvular Regurgitation Paired Analysis



1 Year KM Survival by 30-Day PVL



Numbers at Risk		Months				
	0	3	6	9	12	
None / Trace	351	339	321	309	219	
Mild	191	186	177	168	110	
Mod / Severe	16	15	12	11	9	

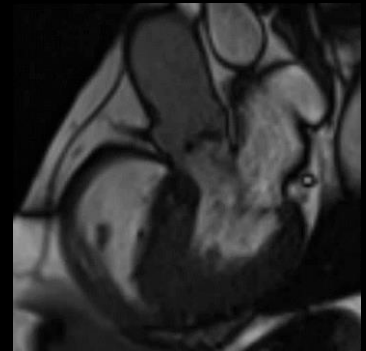


Conclusions

- **Moderate/severe PVR** occurs in 2-15% of patients and is an independent predictor of mortality
- **Severe PVR** is a powerful risk factor for mortality
- **Moderate PVR** is generally associated with worse outcomes but may be better tolerated in patients with pre-existing native AR

Conclusions

- **Mild PVR** is frequent (7-70%) following TAVI and is generally well tolerated
- **Mild PVR** may have an impact on mortality if it is underestimated or if it occurs in a patient with no pre-existing AR and/or restrictive LV physiology
- Decision to perform additional corrective procedures should be individualized according to: severity of PVR, vulnerability factors to AR, and risk factors for complications



**IF YOU FAIL TO PREPARE
BE PREPARED TO FAIL!**

Winston Churchill