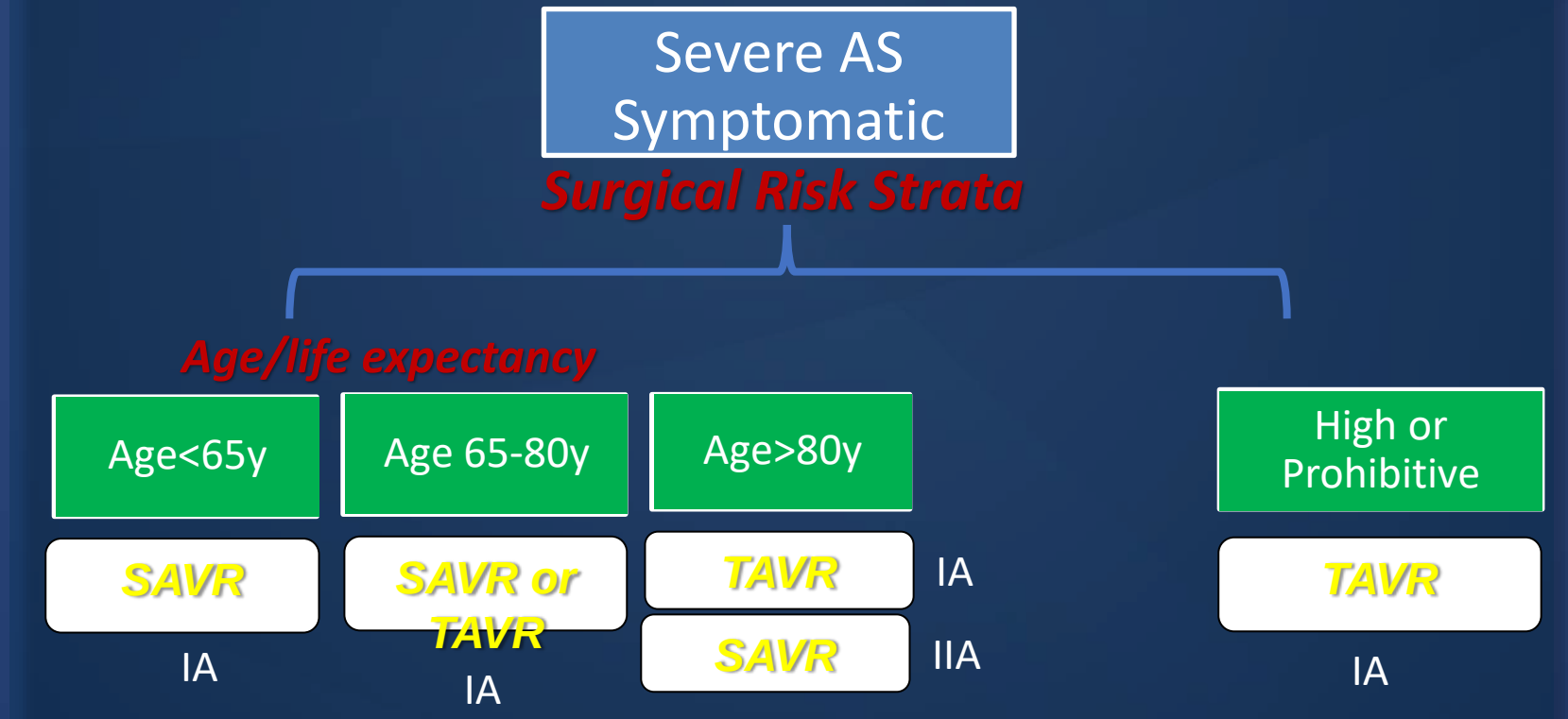
TAVR

Transcatheter Aortic Valve Replacement

ACC/AHA TAVR Guidelines 2020

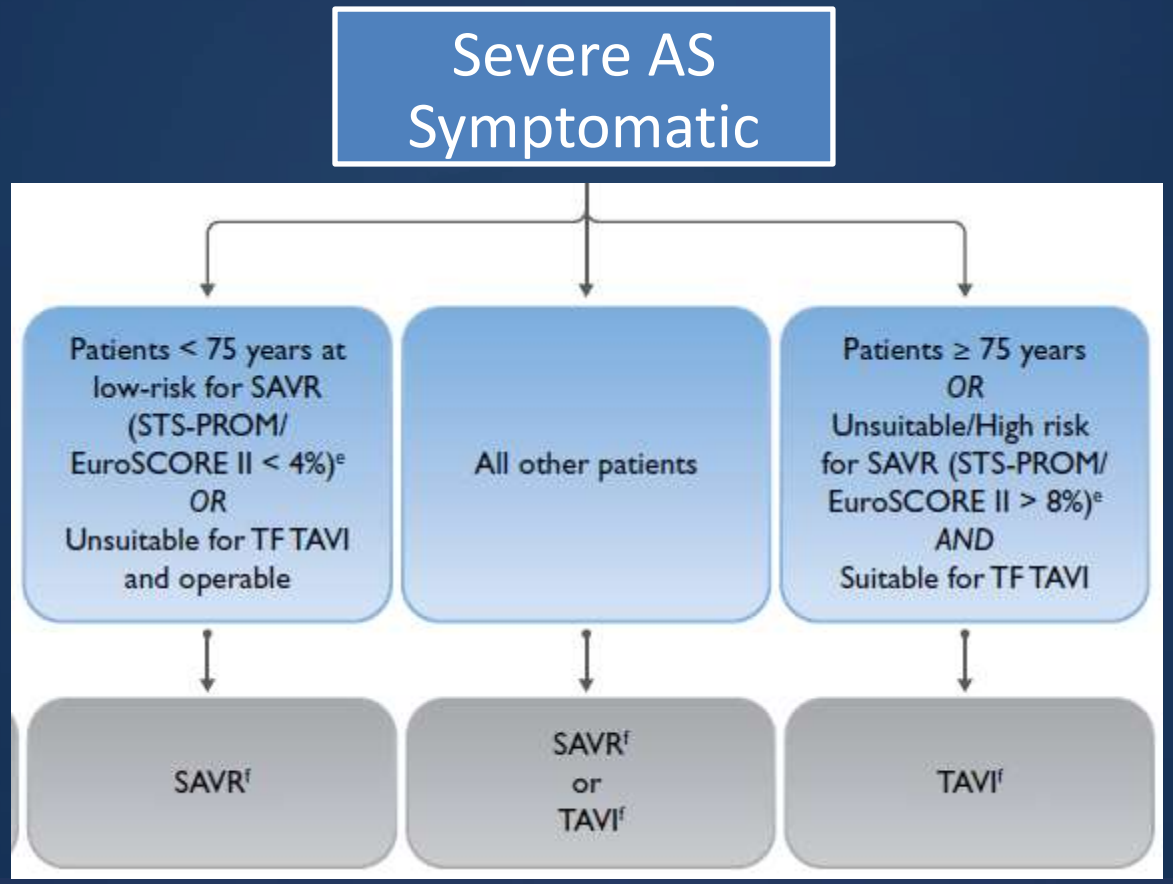
2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease

A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

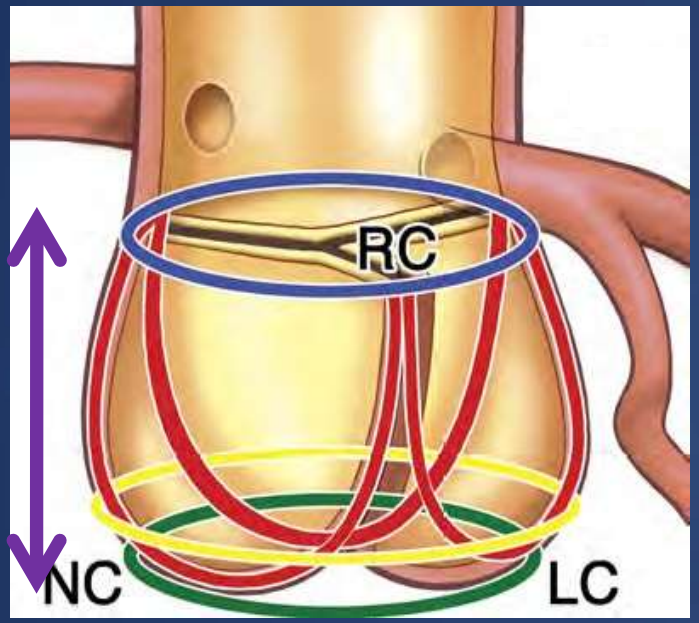


ESC TAVR Guidelines 2021

2021 ESC/EACTS Guidelines for the management of valvular heart disease



Aortic Root Anatomy



Sinotubular junction

Aortic leaflets

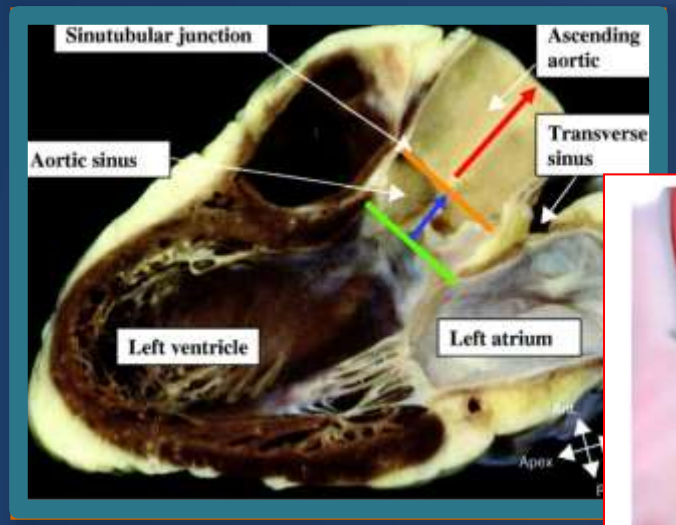
Aortic Annulus

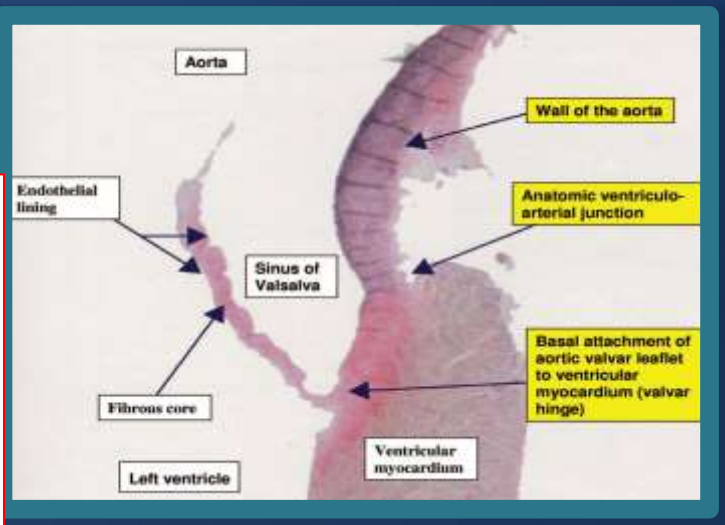
AVA-coronary height

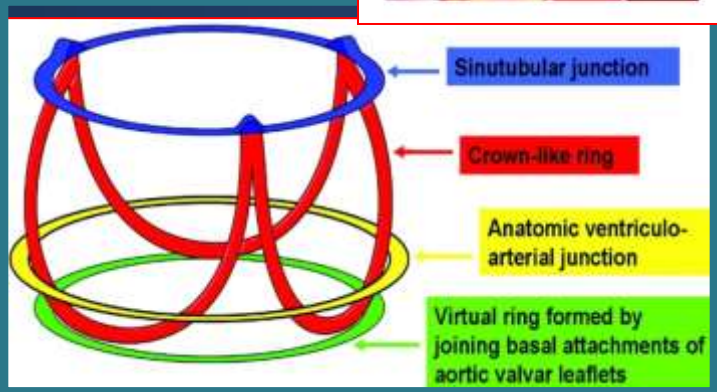
RC = Right coronary cusp; NC = Non-coronary cusp; LC = Left coronary cusp

Valve size should be based on the largest diameter of the AV annulus

Anatomy of Aortic Valvular Complex





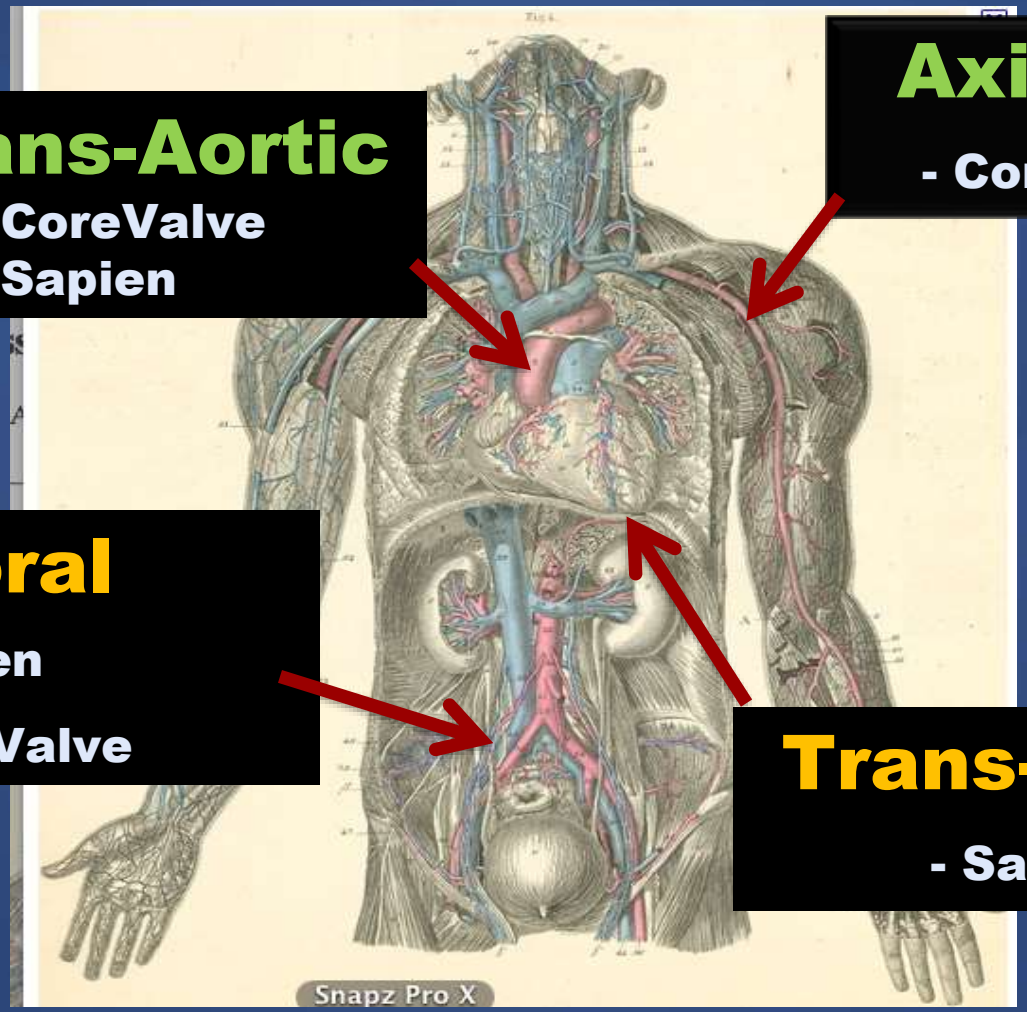


Stability of valve probably determined by the "virtual ring"

Aortic Root thus composed of 3 rings and one crown-like ring

Piazza, N. et al. Circ Cardiovasc Intervent 2008;1:74-81

Access Routes For TAVR



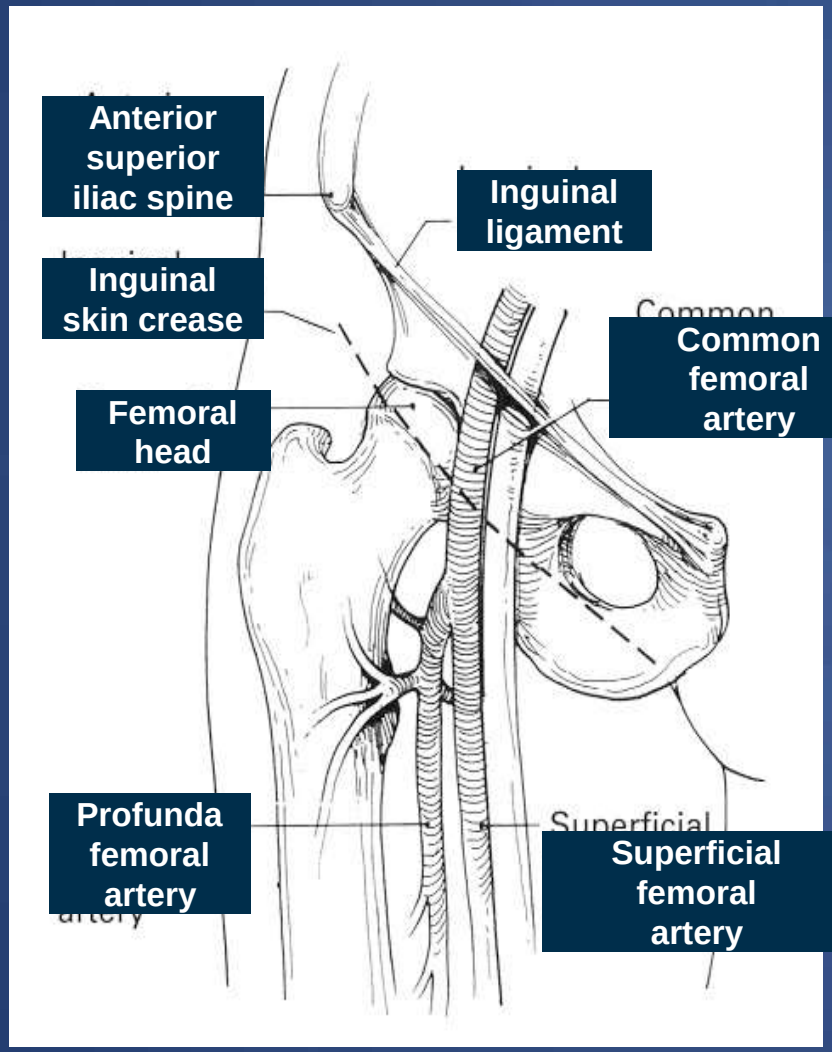
Trans-Aortic
- CoreValve
- Sapien

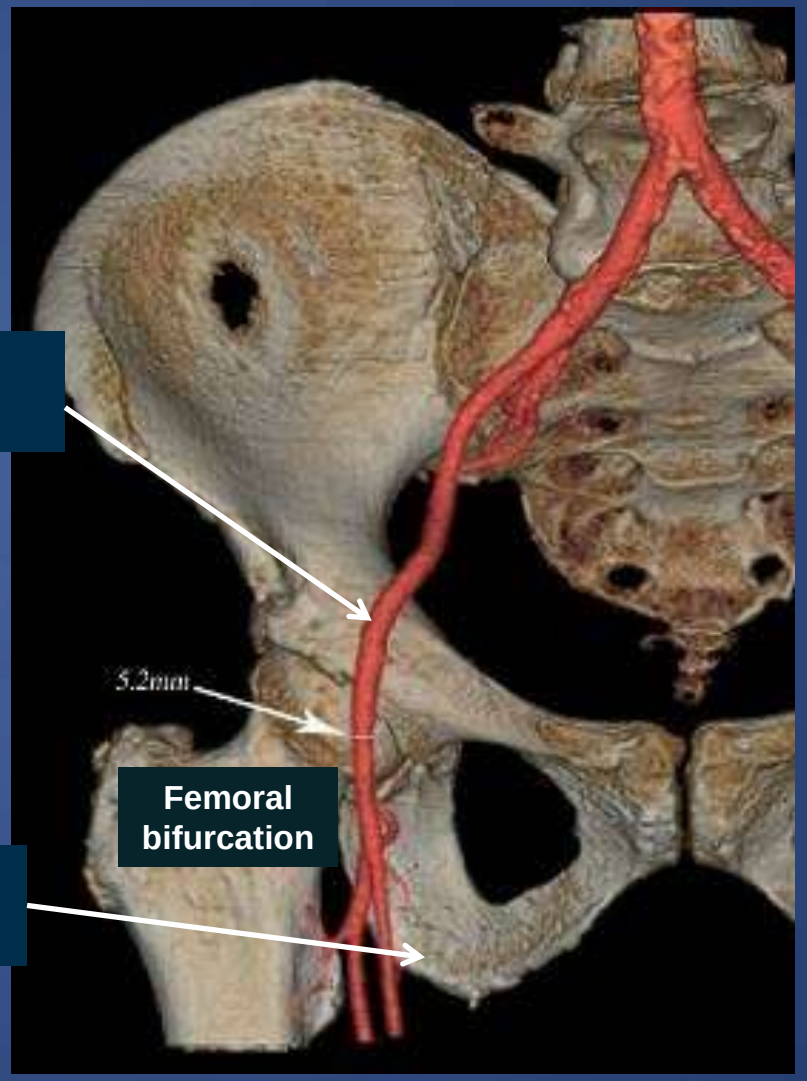
Axillary
- CoreValve

Femoral
- Sapien
- CoreValve

Trans-apical
- Sapien

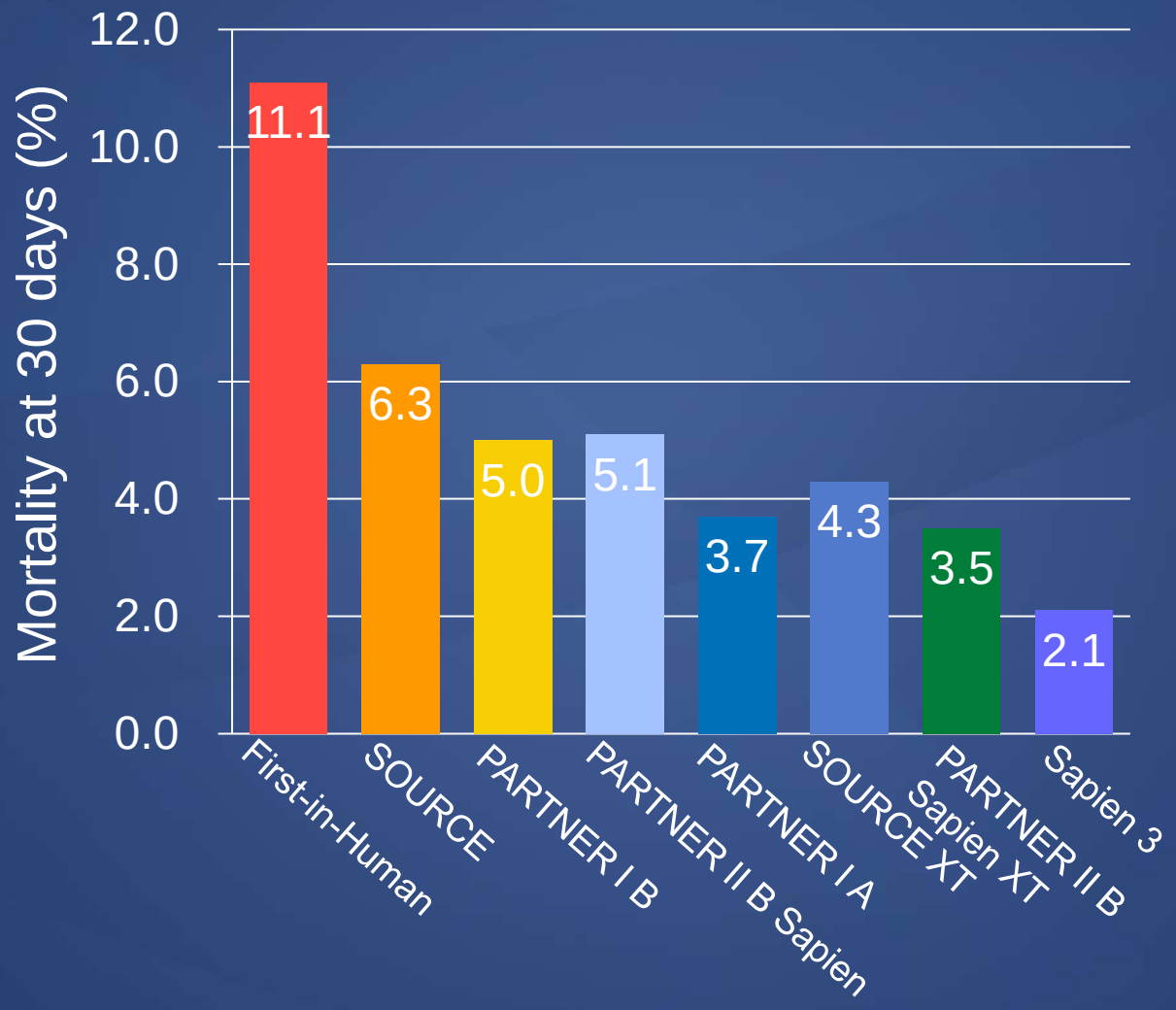
Femoral Artery Anatomy





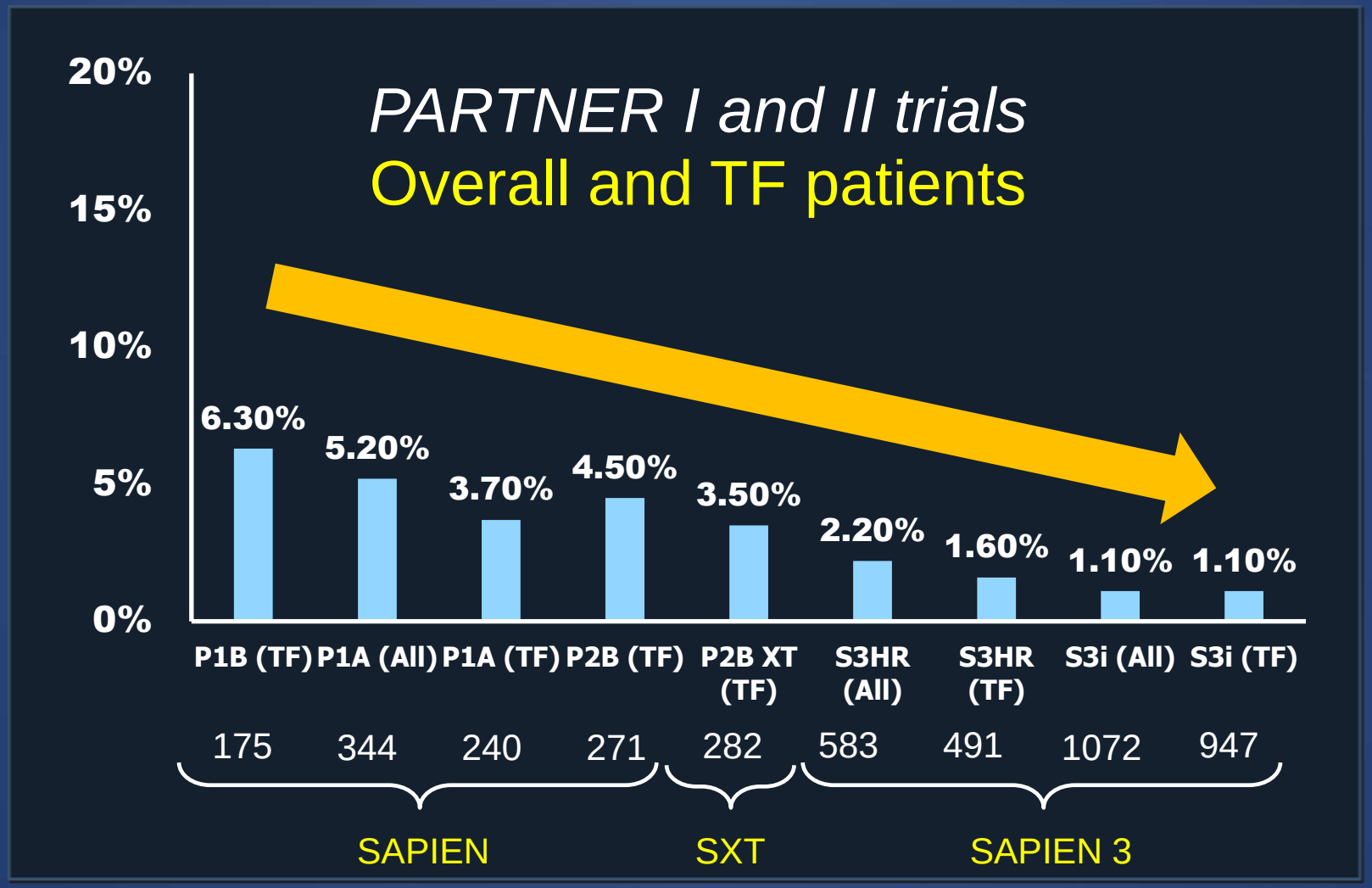
Trend of TAVR

Mortality Across TAVR Studies

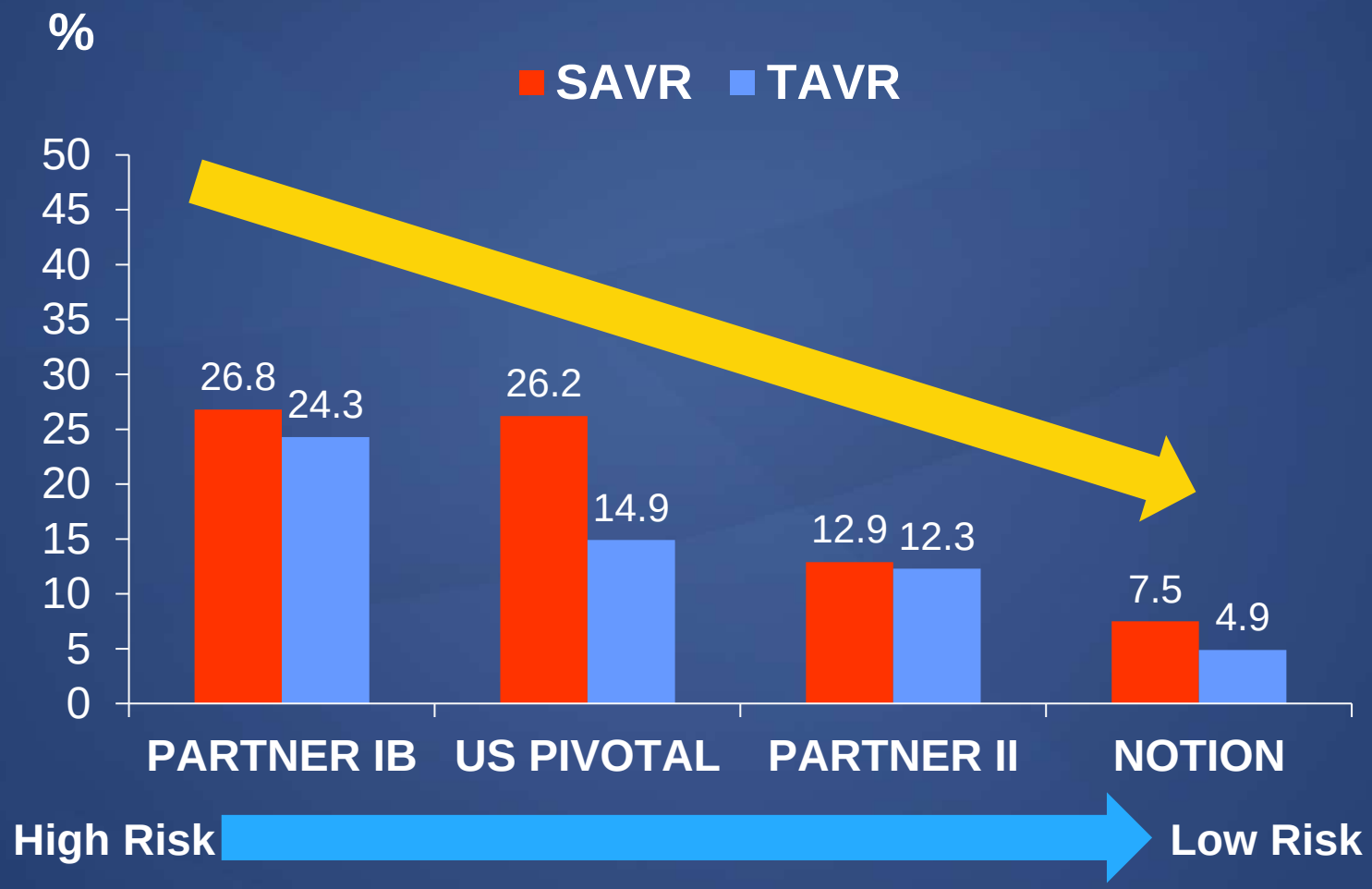


All-Cause Mortality at 30 Days

Edwards SAPIEN Valves



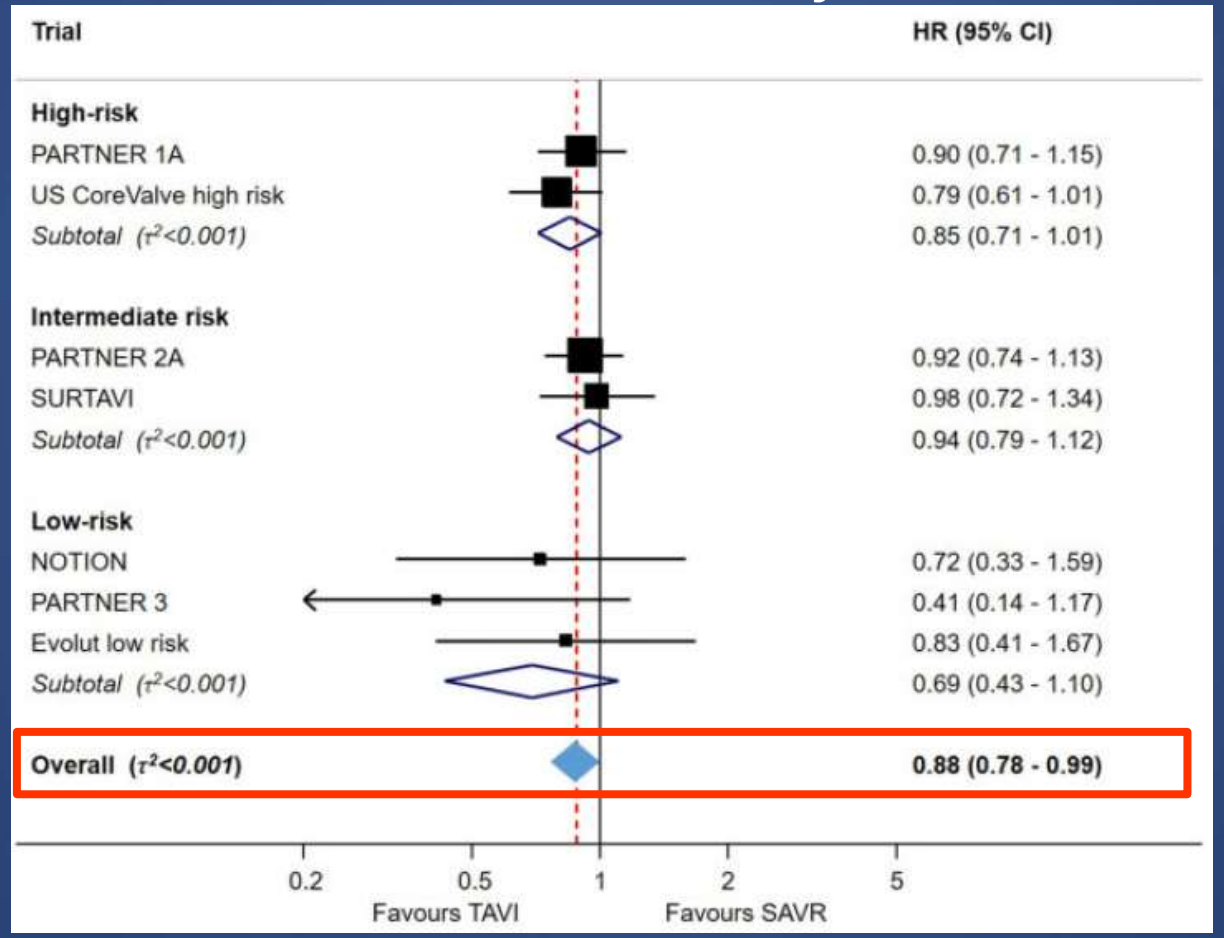
All Cause Mortality @ 1 Year



Metaanalysis From Randomized Trials

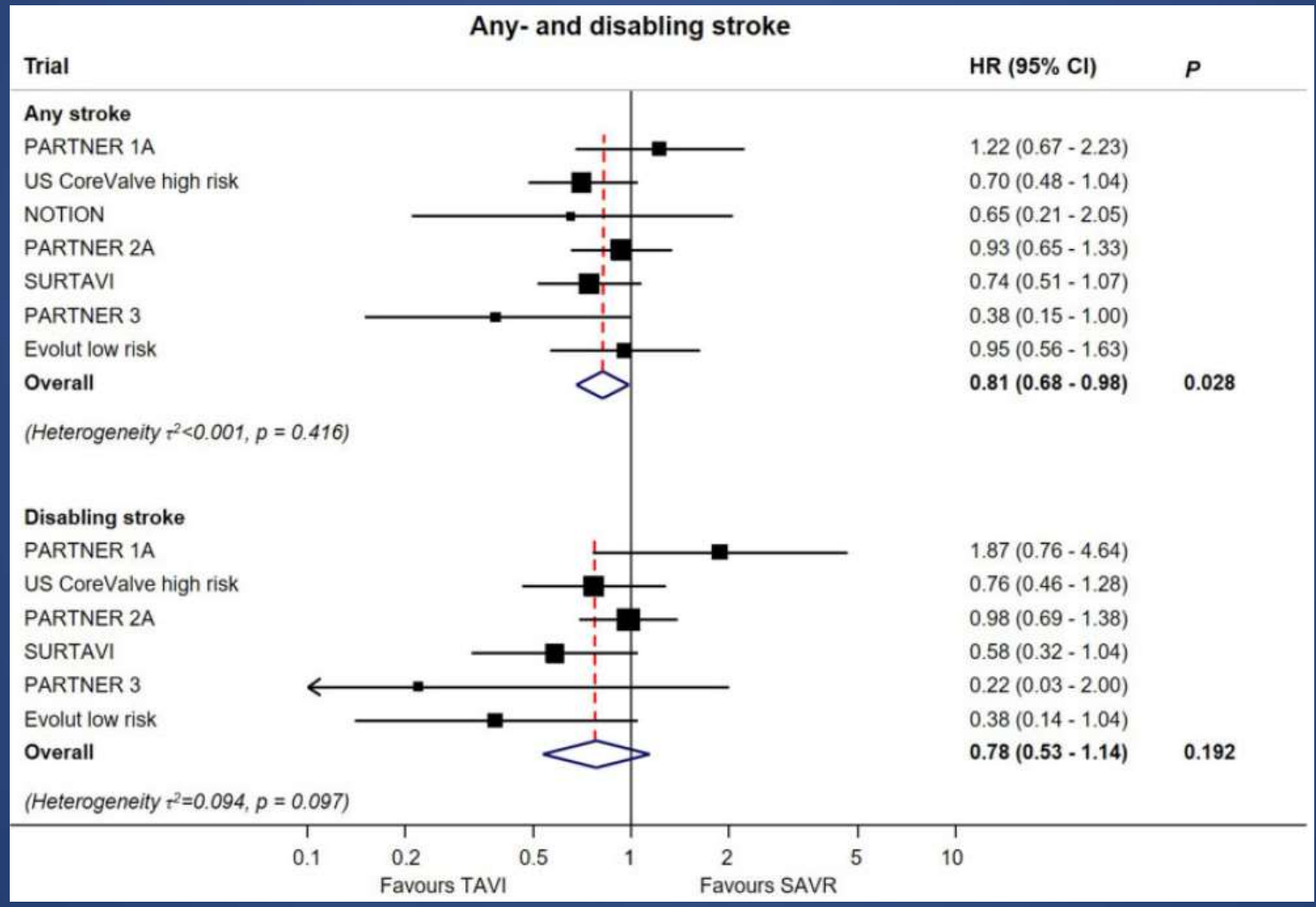
Survival Benefit In TAVR

All-cause mortality



Siontis GC et al Eur Heart J European Heart Journal (2019) 40, 3143–3153

Metaanalysis From Randomized Trials



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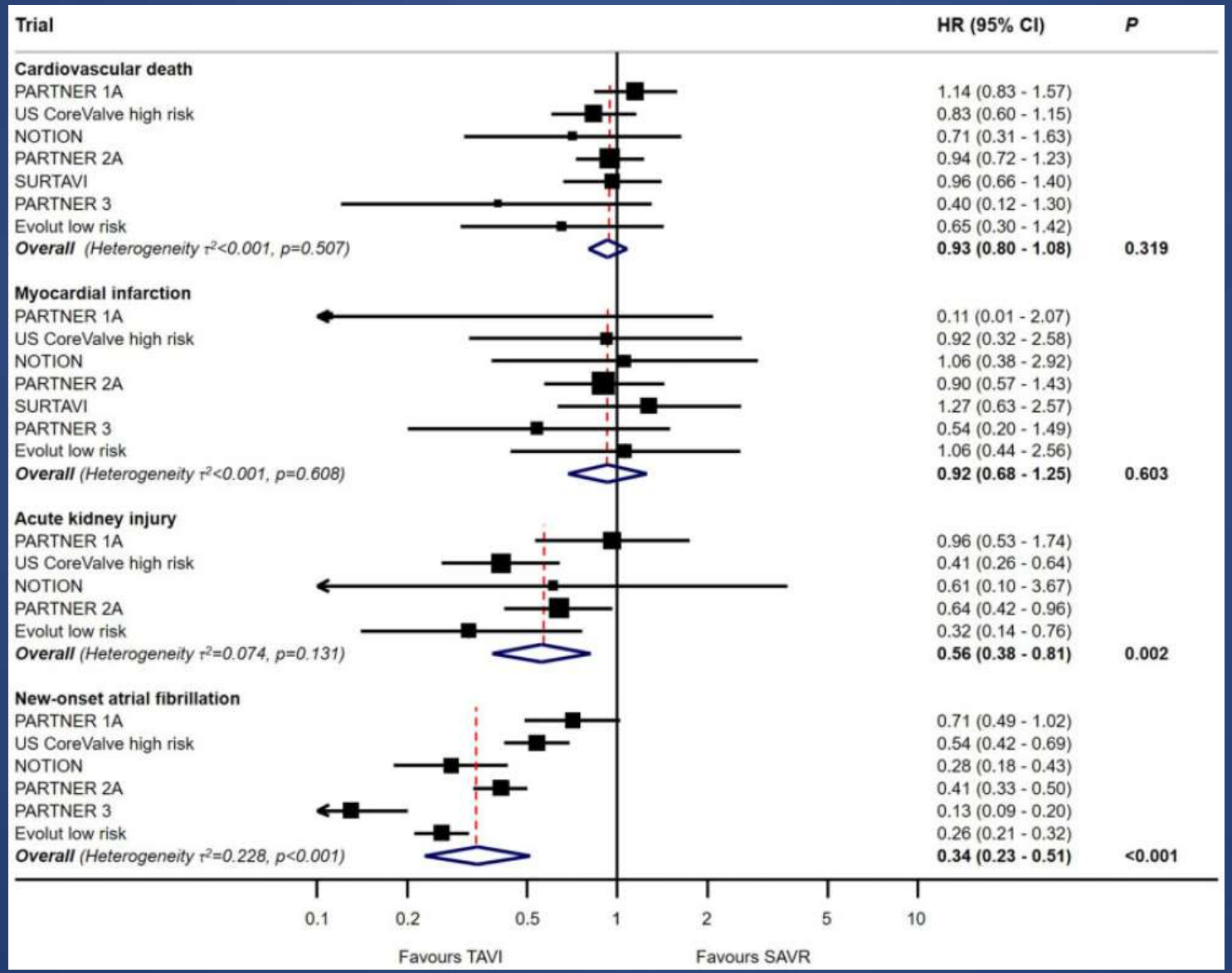
Metaanalysis From Randomized Trials

Analyses for the secondary outcomes



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Metaanalysis From Randomized Trials

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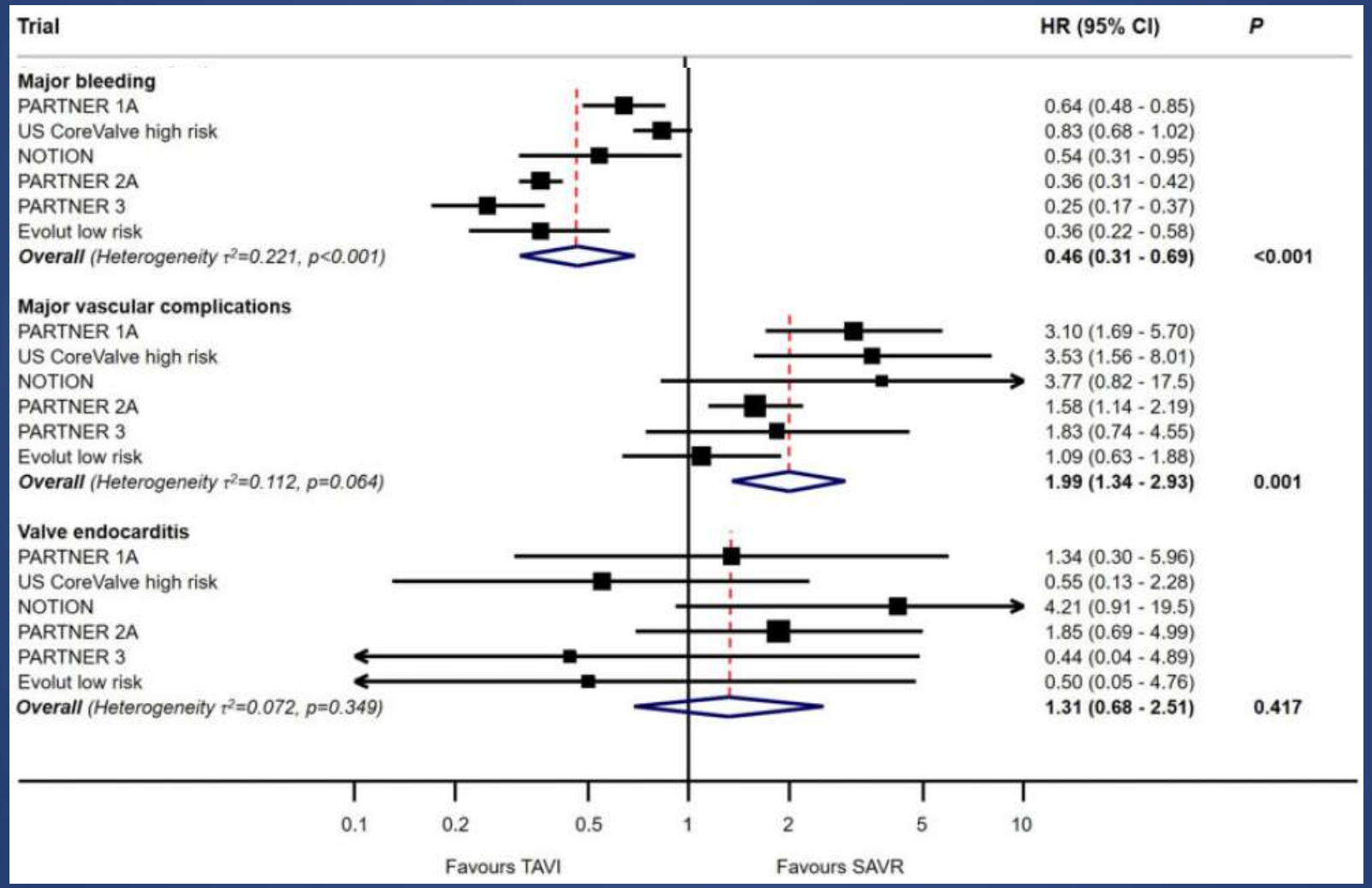


Siontis GC et al Eur Heart J European Heart Journal (2019) 40, 3143–3153

Functional Classification of Symptomatic Severe AS Patients

Prohibitive Surgical Risk, ***Inoperable***

	STS Score	Proportion
High Risk	***> 8%***	~10%
Intermediate Risk	***4~8%***	10~25%
Low Risk	***< 4%***	~70%

RCT of TAVR:
Chain From High to Low-Risk

Trial Name	STS Score	Age
Inoperable Population		
PARTNER IB Trial	11.6	83
High Risk Population		
PARTNER IA Trial	11.8	84
CoreValve US Pivotal Trial	7.4	83
Intermediate Risk Population		
PARTNER IIA Trial	5.8	82
SURTAVI	4.4	80
Low Risk Population		
NOTION Trial	3.0	79
PARTNER III	1.9	74
Evolut Low Risk Trial	1.9	74

Innovation in TAVR
Remaining Clinical Needs

- Bicuspid AV disease
- AS + concomitant disease (CAD, MR, AF)
- Severe asymptomatic AS
- Moderate AS + CHD
- Durability concerns (including valve leaflet thrombosis) and coronary obstruction/access
- Adjunct Pharmacotherapy
- High-risk severe AR

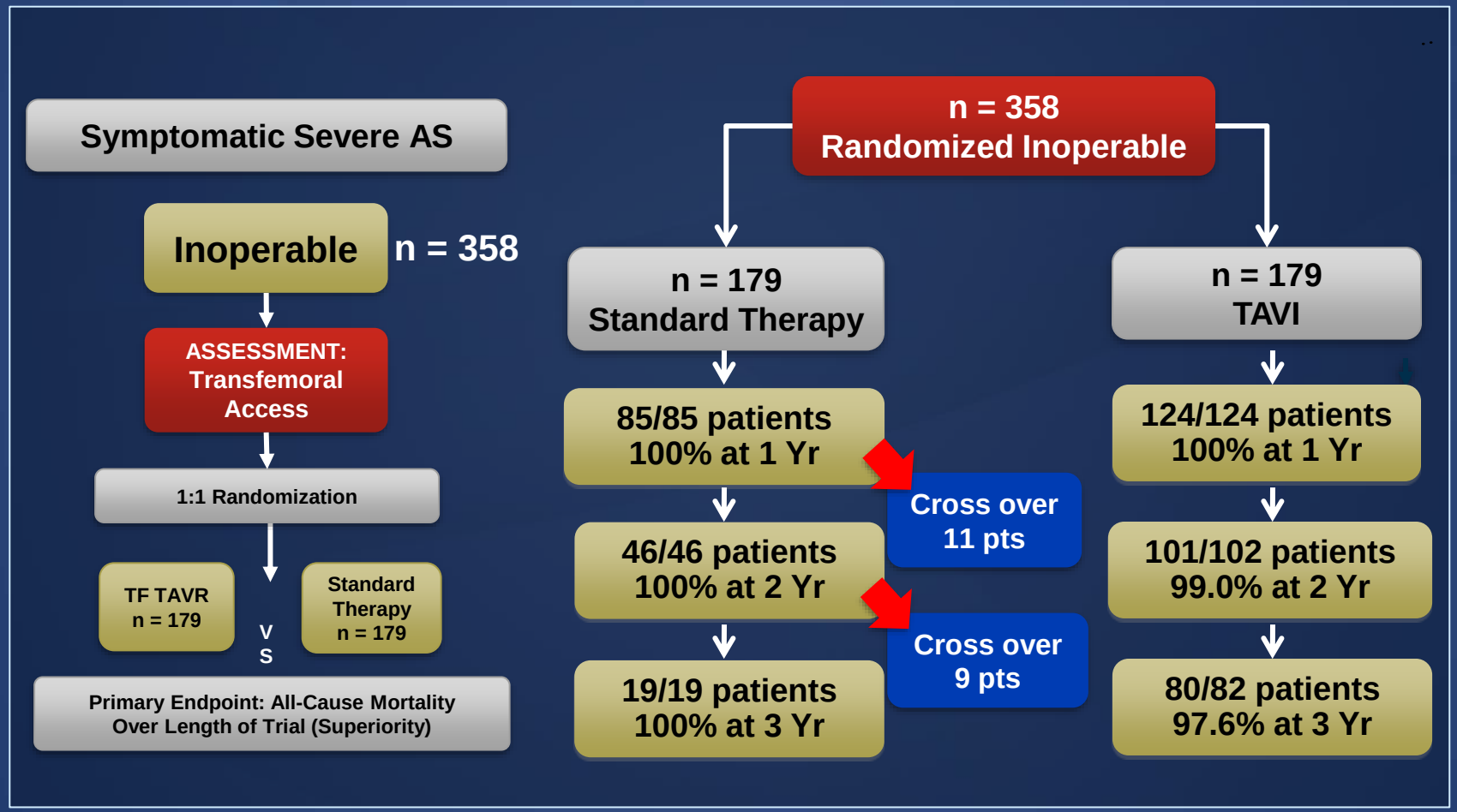
Edwards SAPIEN
balloon-expandable THV

SAPIEN valve trials

PARTNER trial

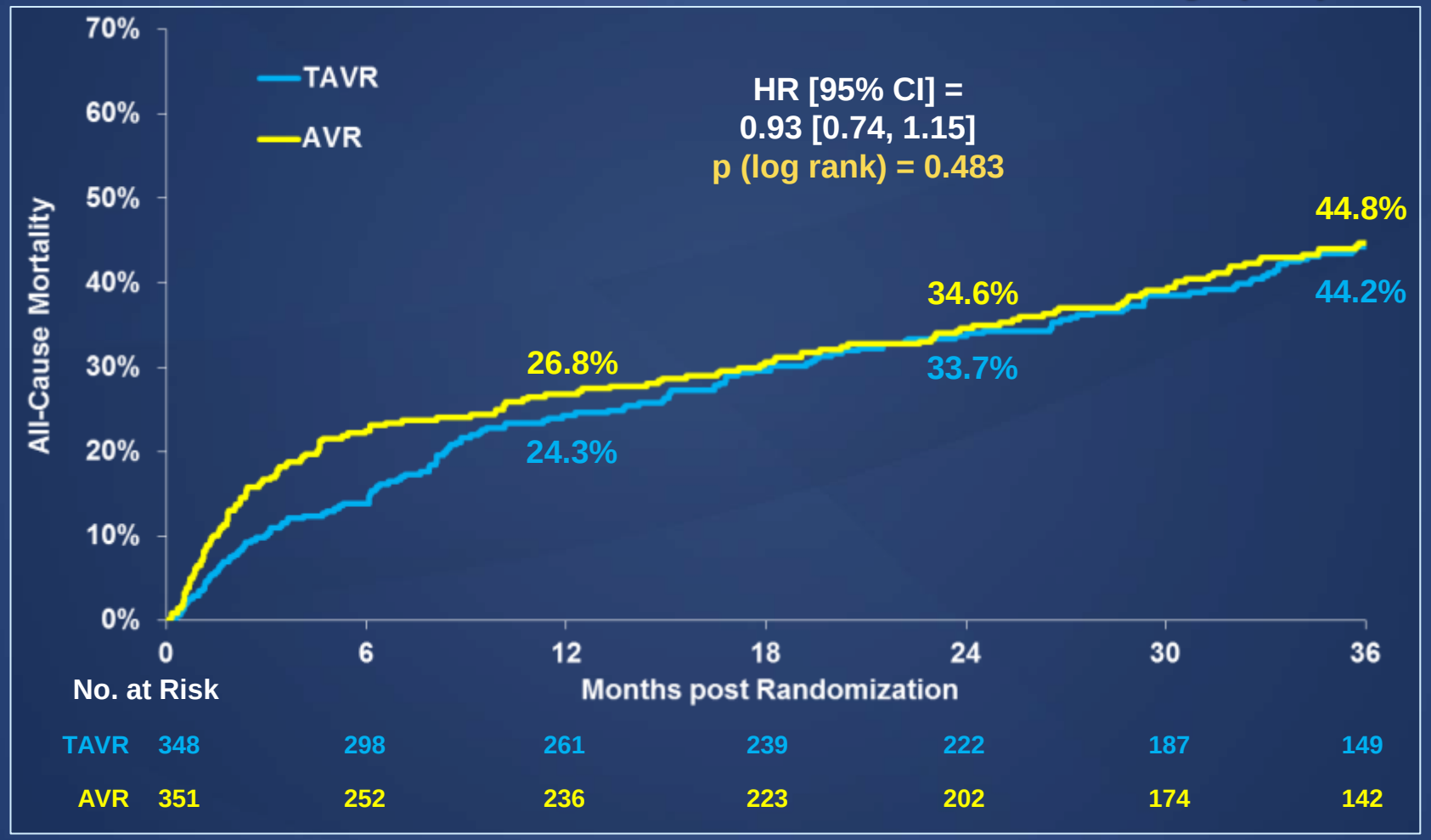
PARTNER trial : Inoperable

3 year follow-up



PARTNER trial : High Risk

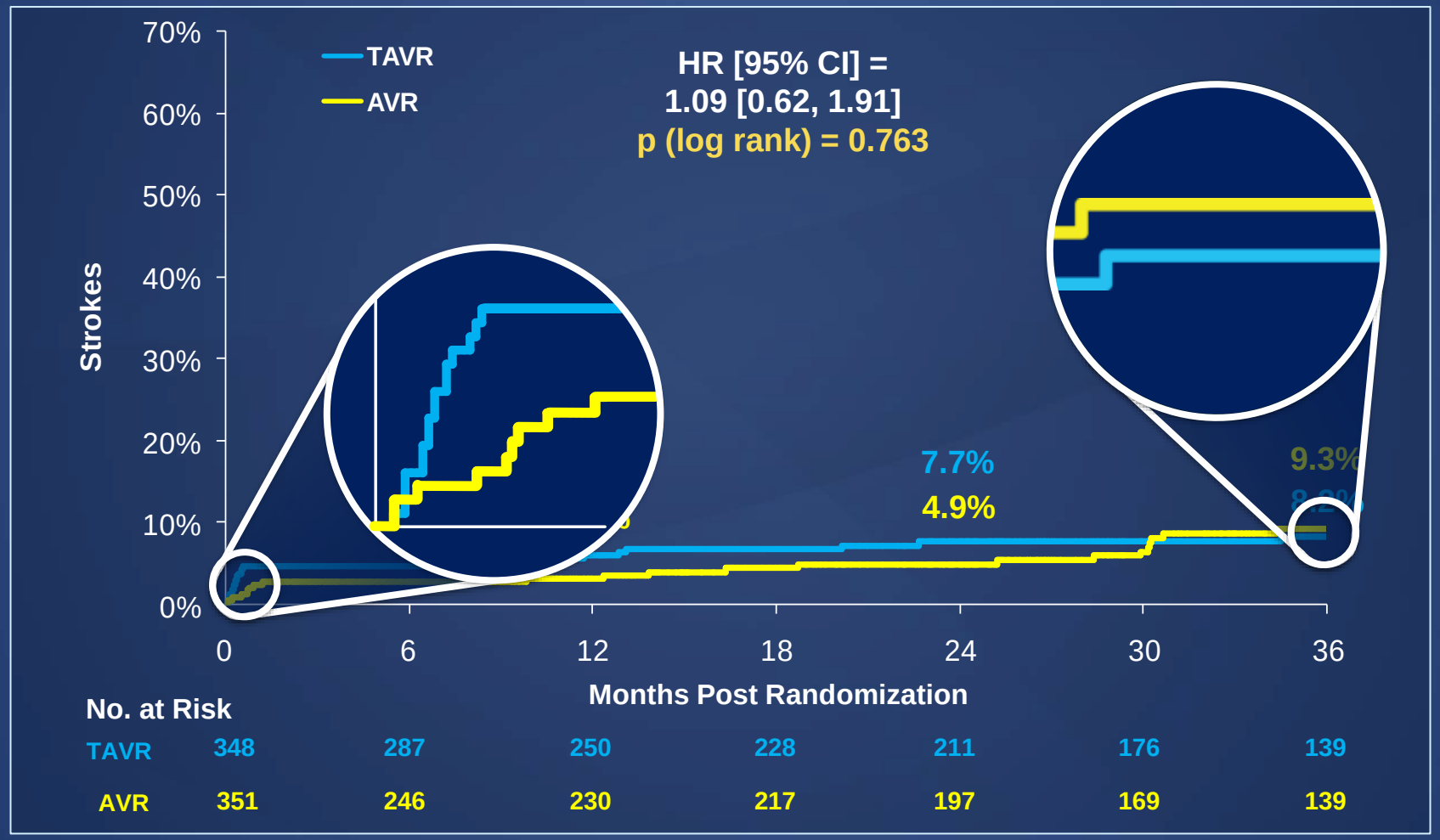
3 year follow-up All-Cause Mortality (IIT)



Vinod H. Thourani et al. ACC 2013

PARTNER trial : High Risk

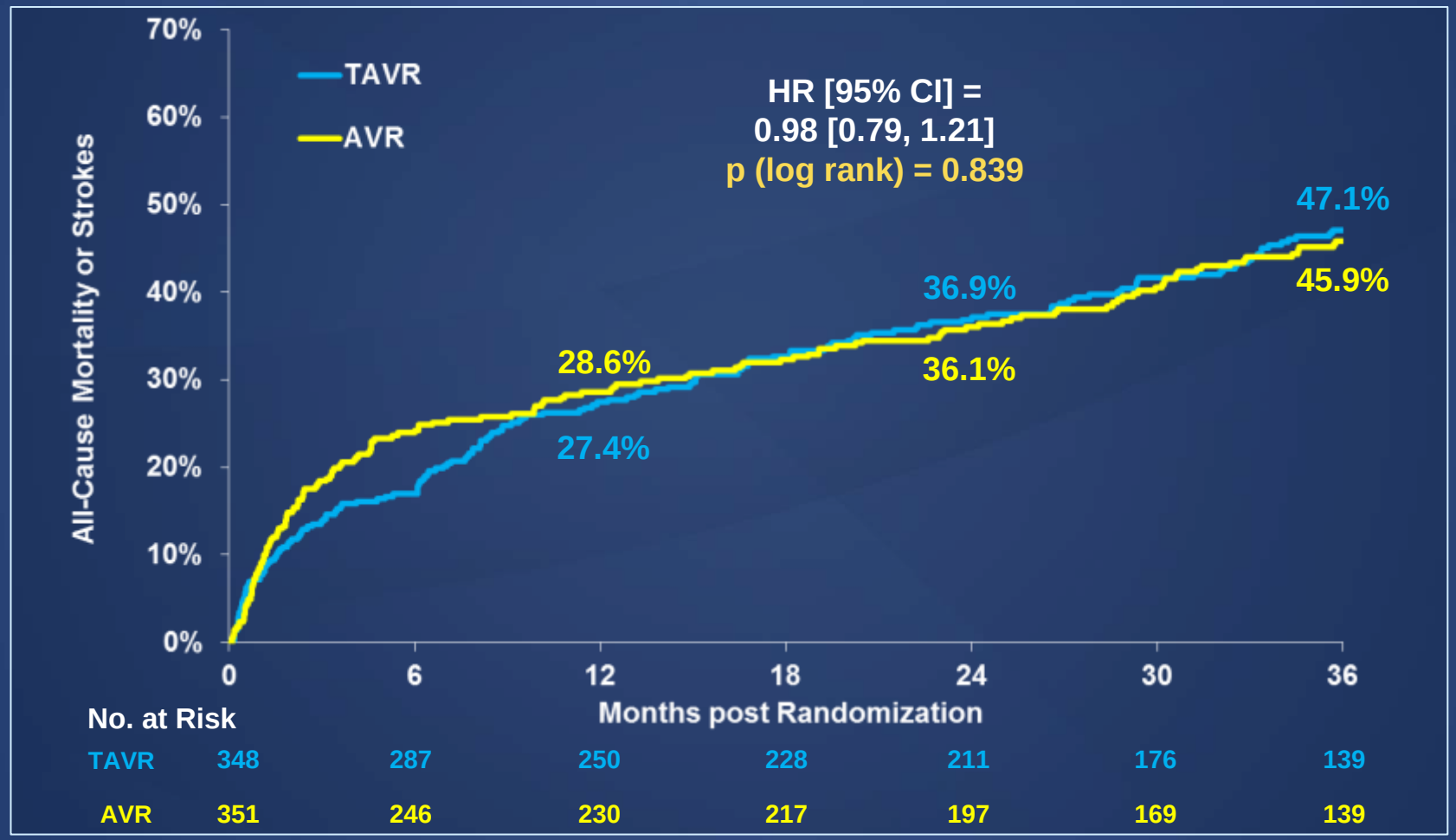
3 year follow-up Stroke (IIT)



Vinod H. Thourani et al. ACC 2013

PARTNER trial : High Risk

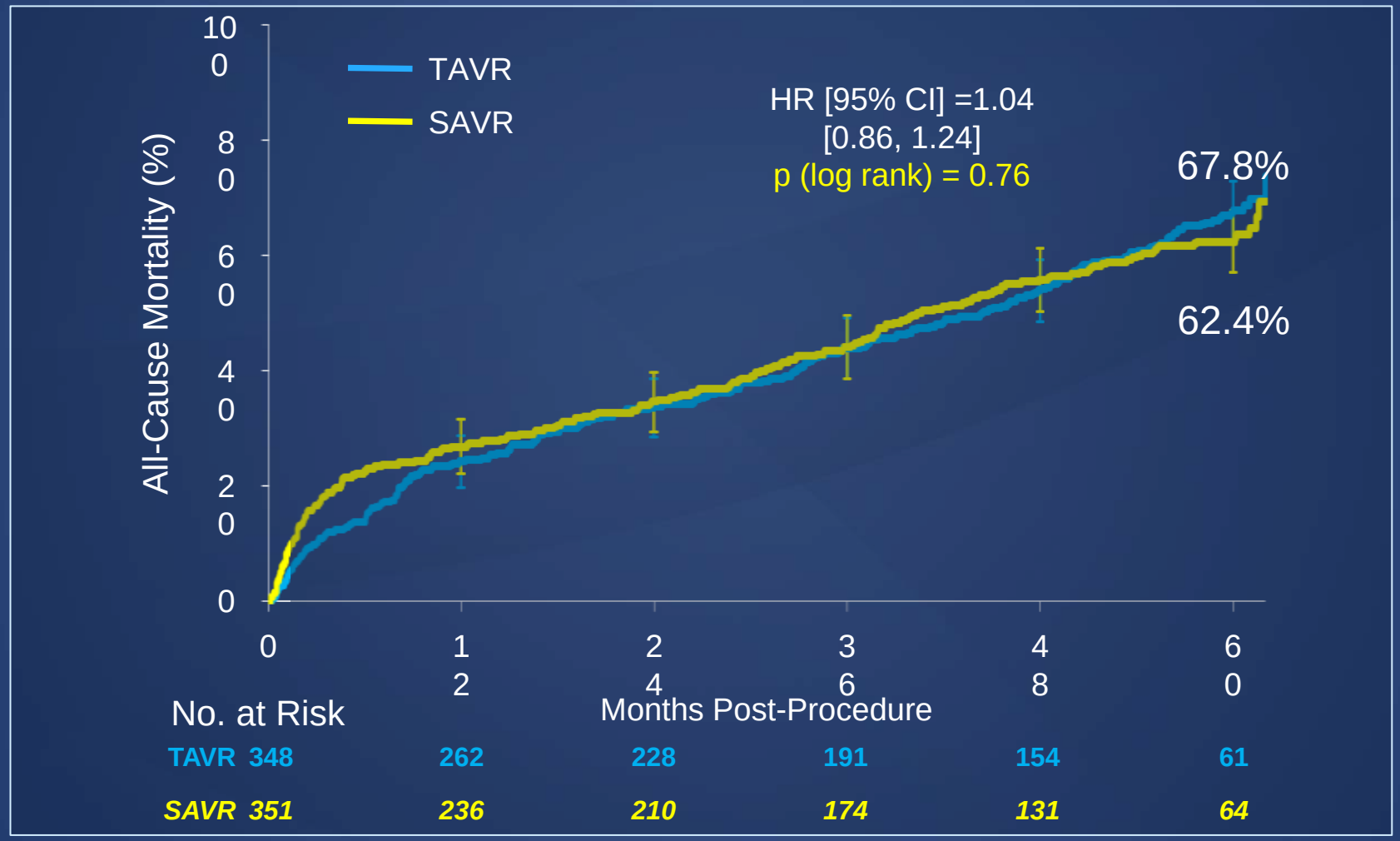
3 year follow-up All-Cause Mortality or Strokes (IIT)



Vinod H. Thourani et al. ACC 2013

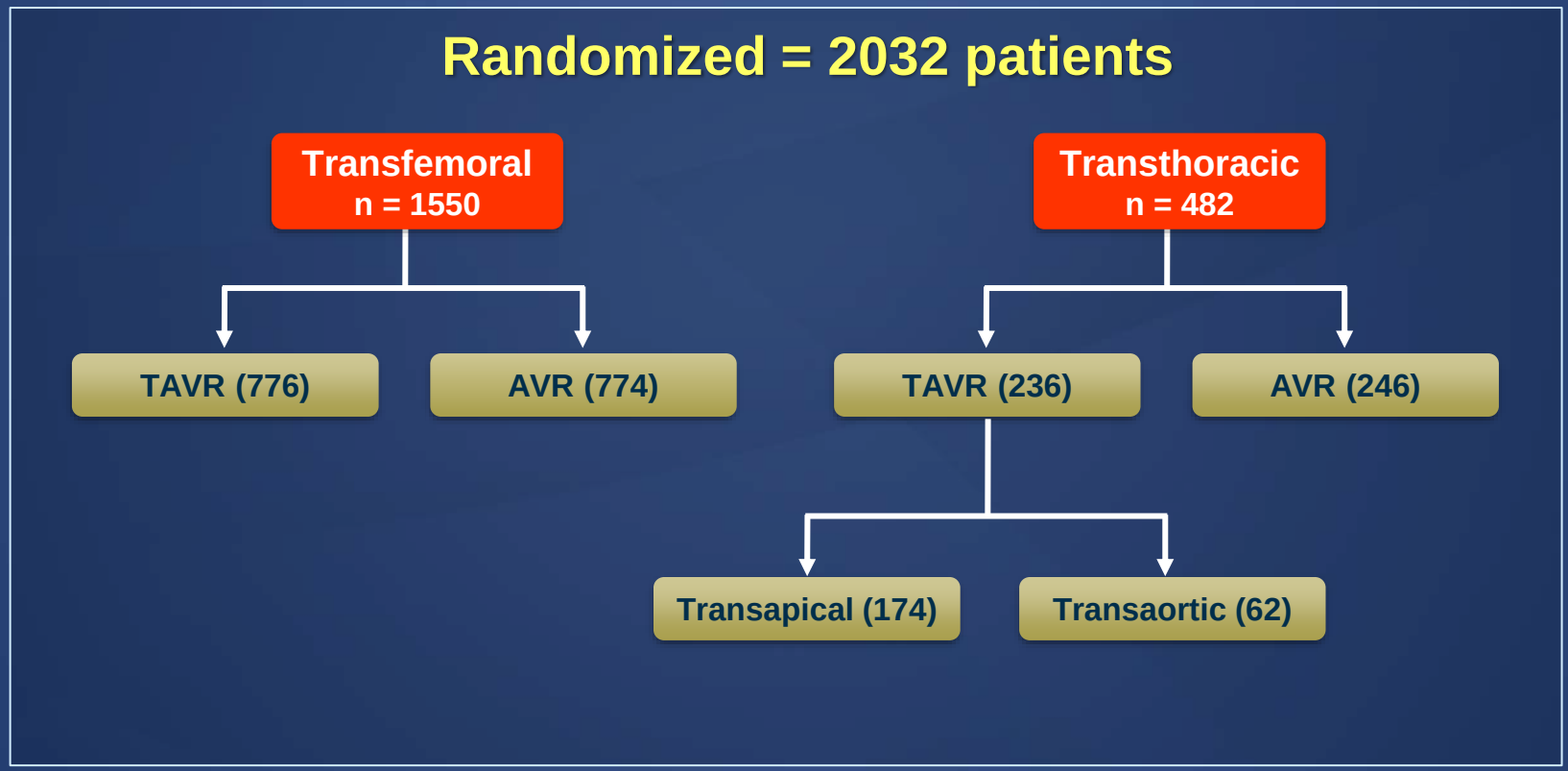
5 Years Outcomes of PARTNER I trial

All-Cause Mortality (ITT)



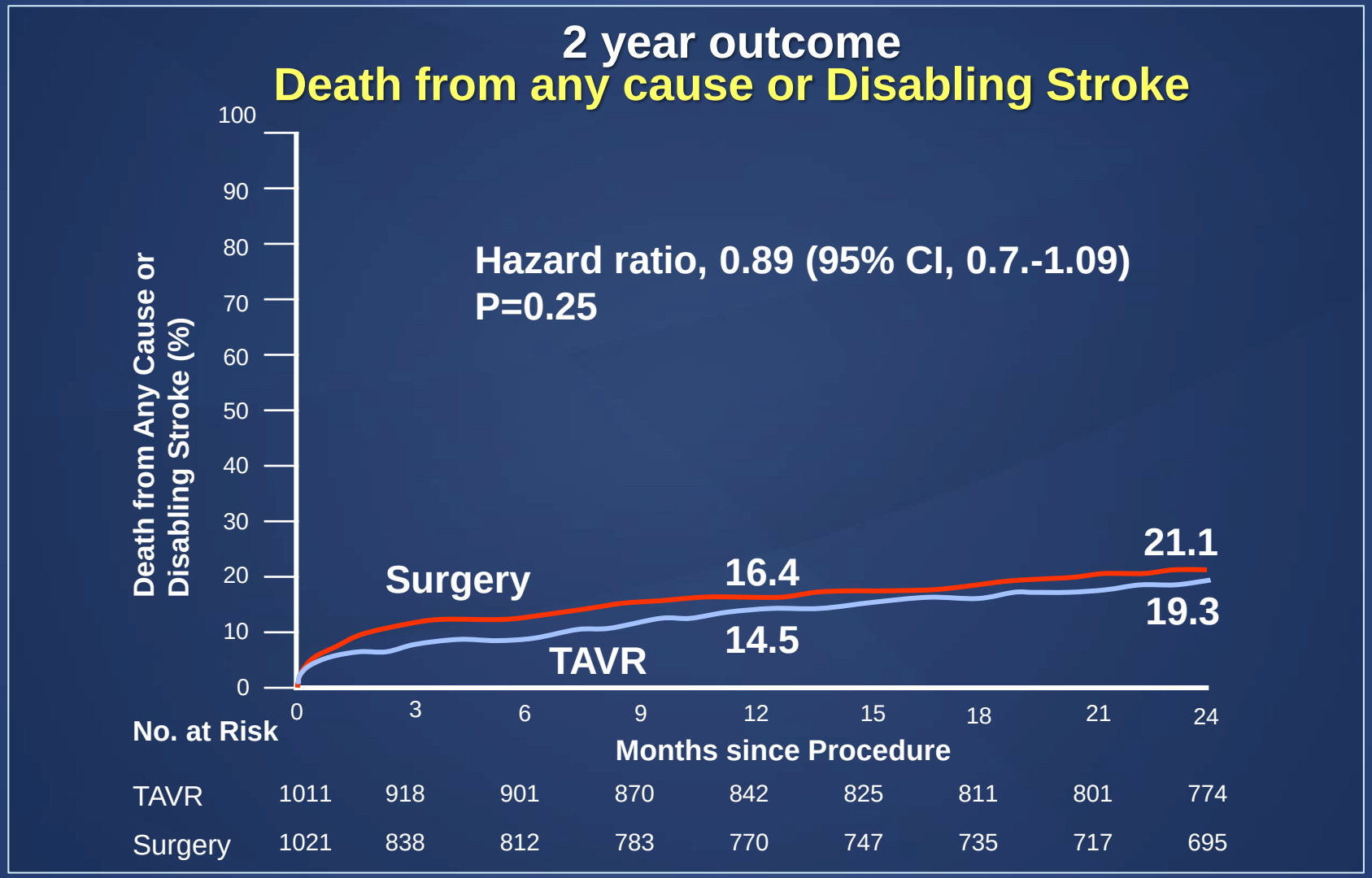
PARTNER 2 trial Cohort A

TAVR (SAPIEN XT) VS AVR
Intermediate risk



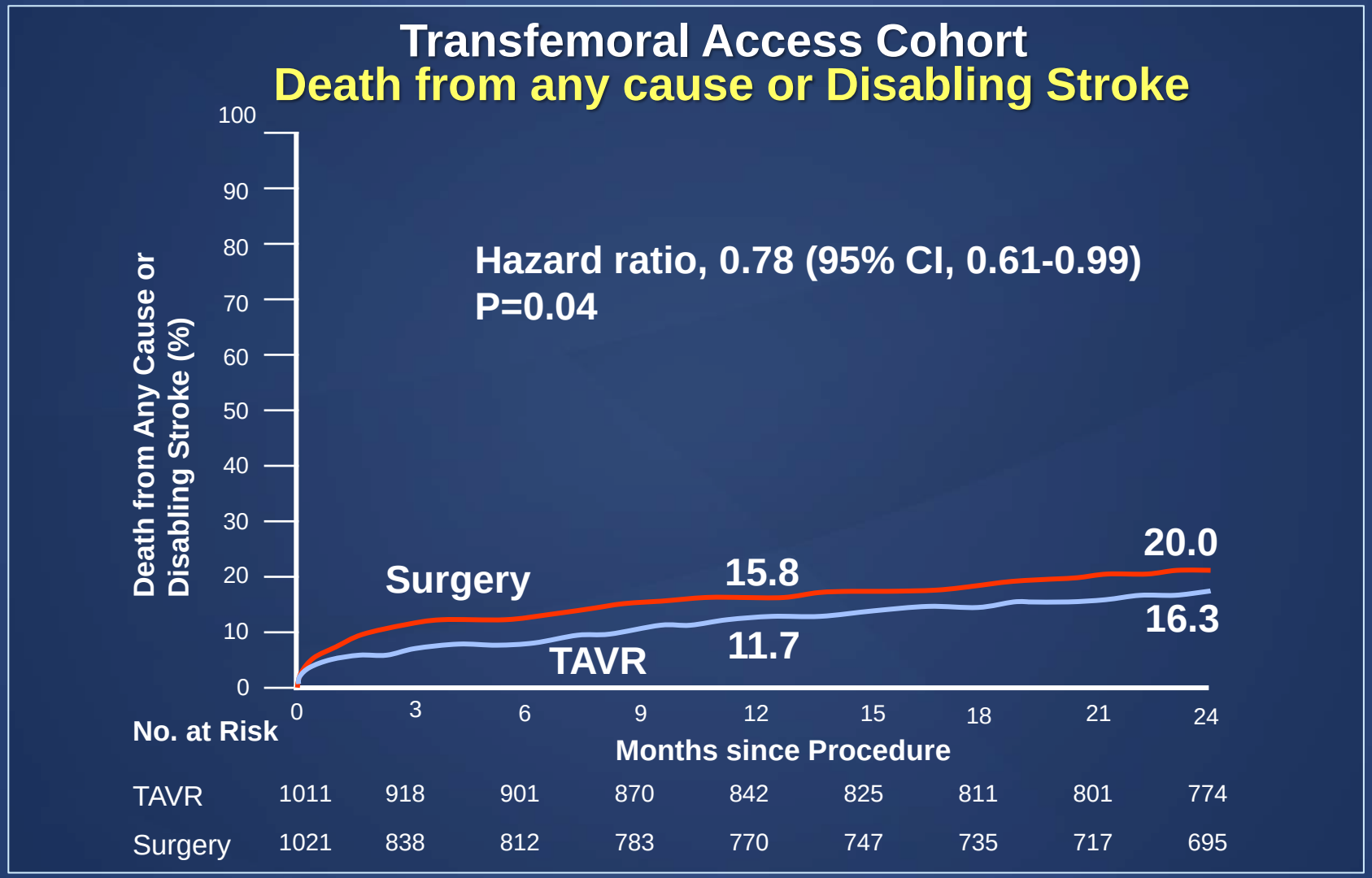
Martin B. Leon et al NEJM 2016

PARTNER 2 trial : Intermediate risk



Martin B. Leon et al NEJM 2016

PARTNER 2 trial : Intermediate risk



Martin B. Leon et al NEJM 2016

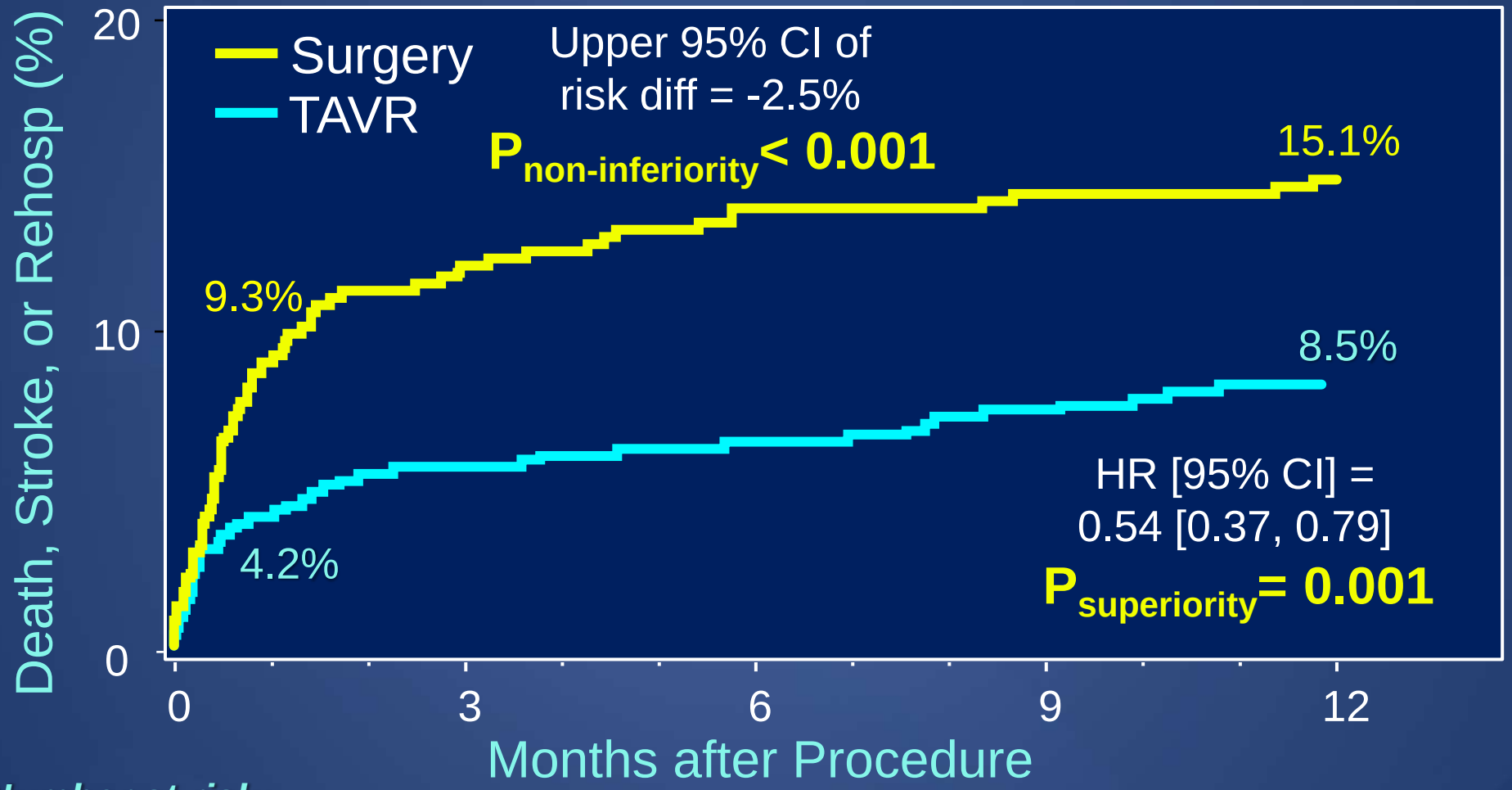
THE PARTNER 3 TRIAL

PARTNER 3

Transcatheter or Surgical Aortic Valve Replacement in Low Risk Patients with Aortic Stenosis

PARTNER 3 trial

Primary Endpoint

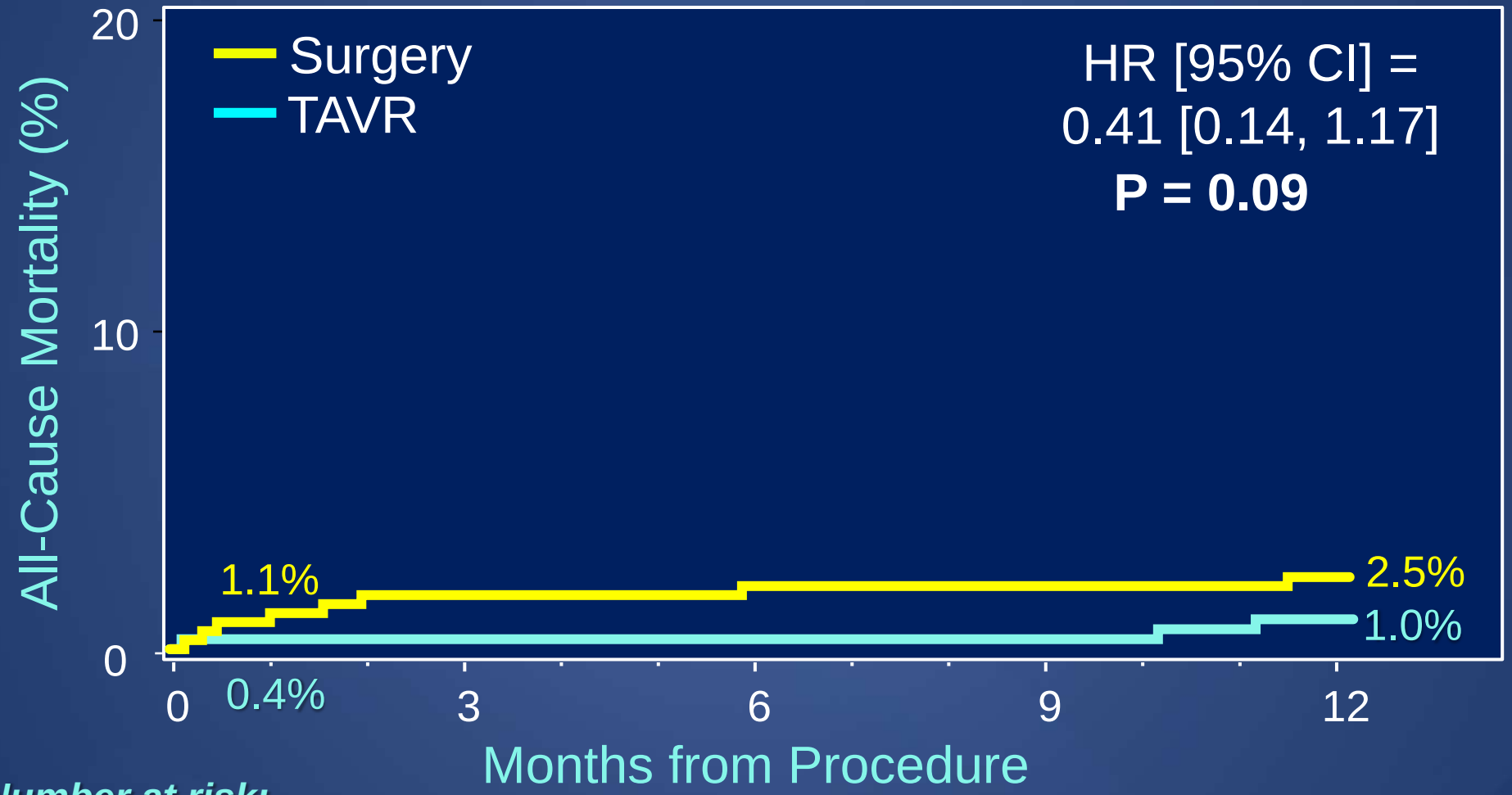


Number at risk:

Surgery	**454**	**408**	**390**	**381**	**377**	**374**
TAVR	**496**	**475**	**467**	**462**	**456**	**451**

PARTNER 3 trial

All-Cause Mortality

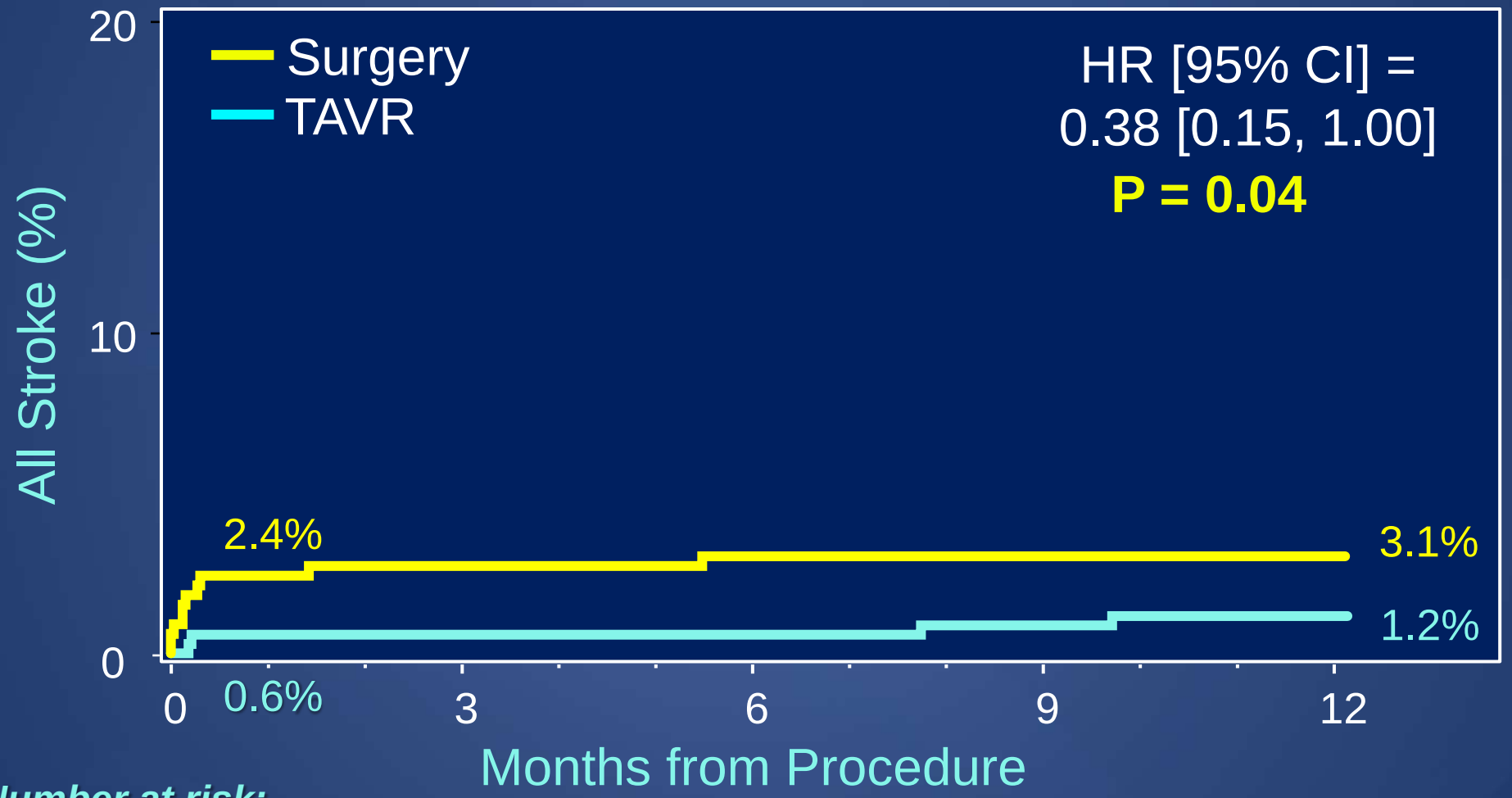


Number at risk:

Surgery	**454**	**445**	**438**	**433**	**431**	**427**
TAVR	**496**	**494**	**494**	**493**	**492**	**488**

PARTNER 3 trial

All Stroke

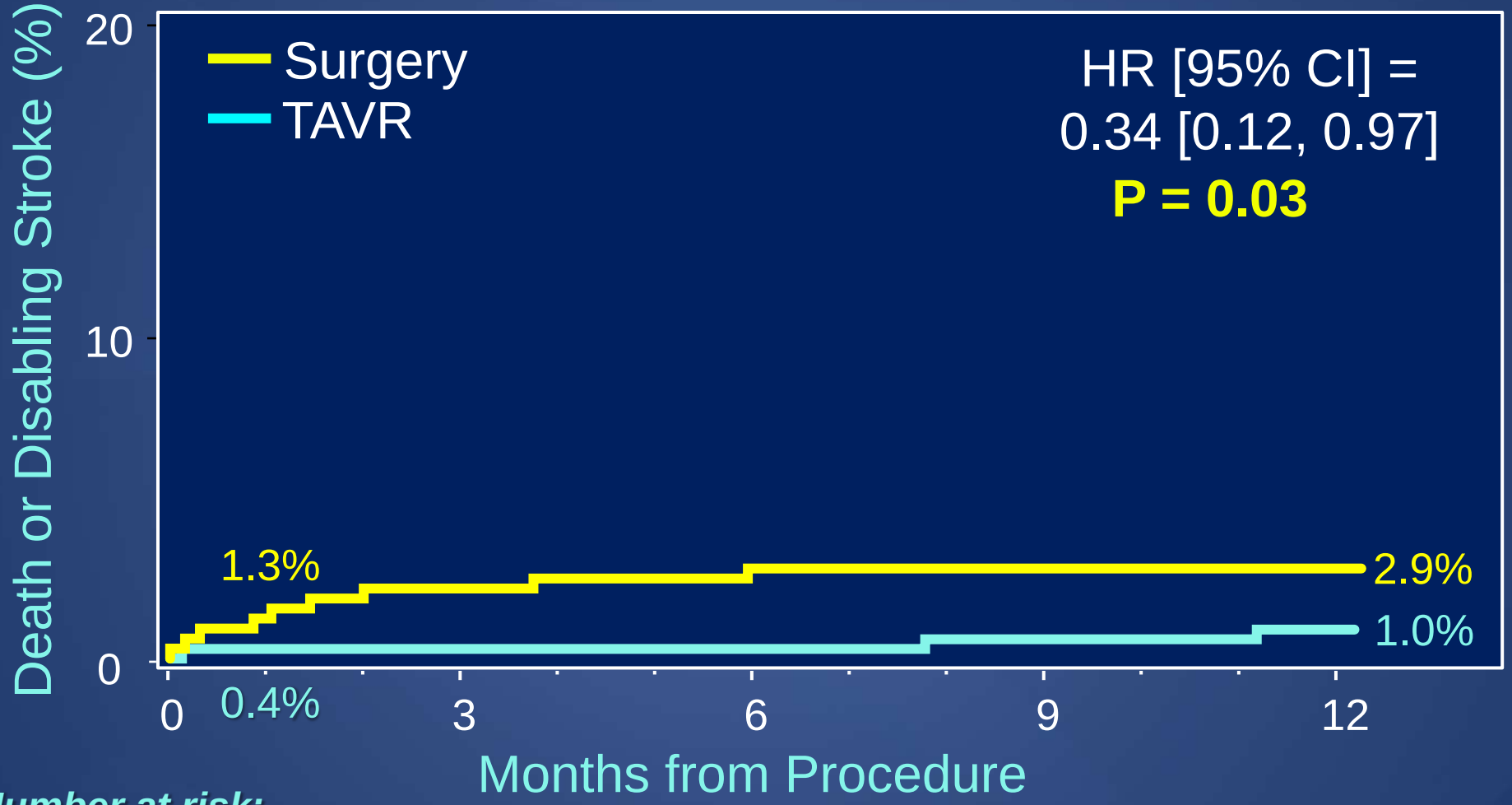


Number at risk:

Surgery	**454**	**435**	**427**	**423**	**421**	**417**
TAVR	**496**	**491**	**491**	**489**	**487**	**484**

PARTNER 3 trial

Death or Disabling Stroke

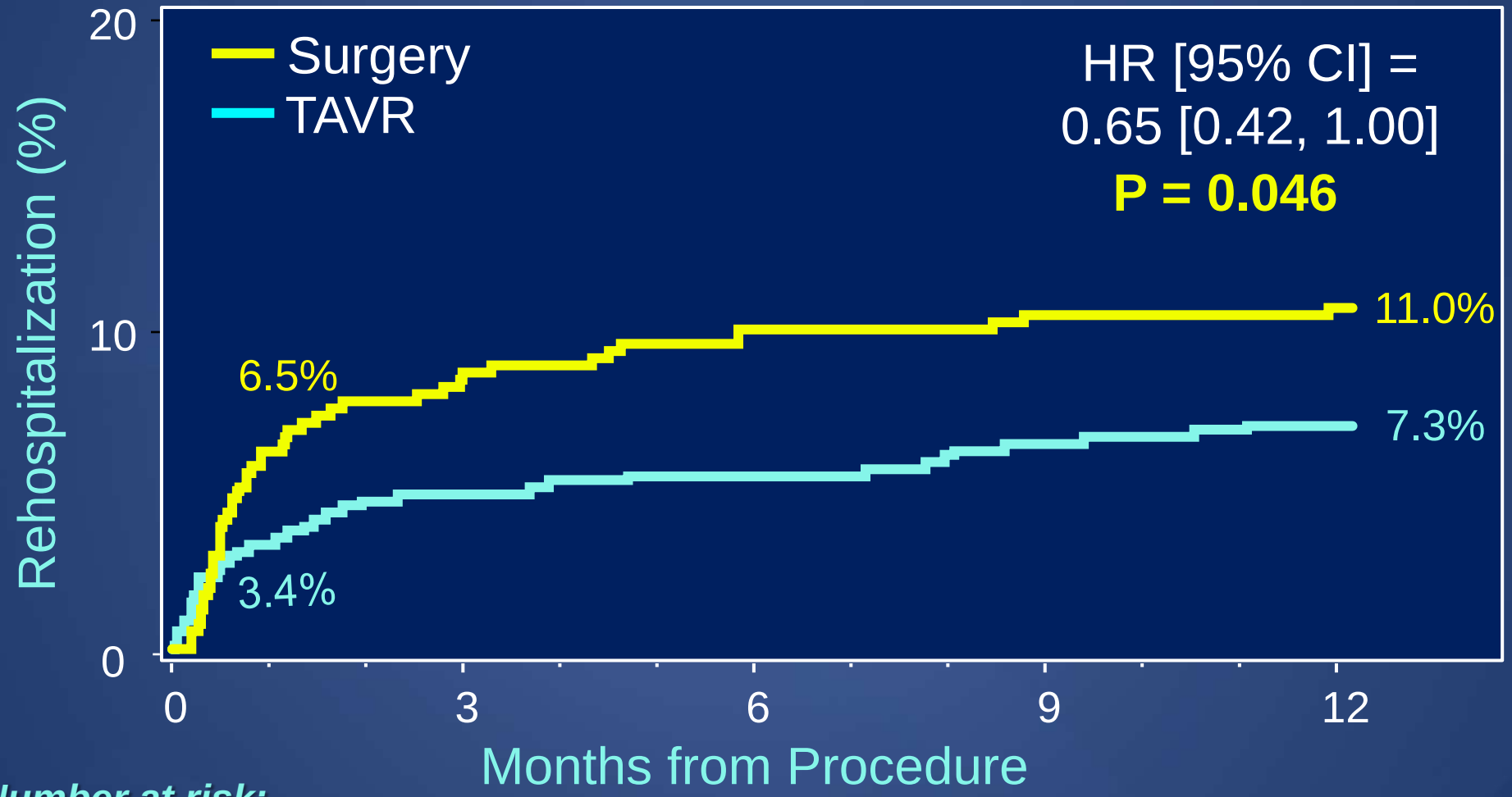


Number at risk:

Surgery	**454**	**444**	**436**	**432**	**430**	**426**
TAVR	**496**	**494**	**494**	**493**	**491**	**488**

PARTNER 3 trial

Rehospitalization



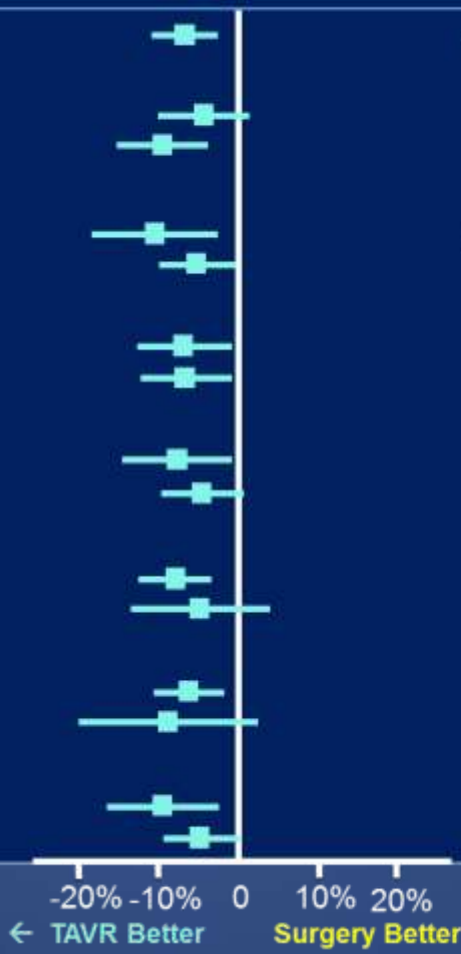
Number at risk:

Surgery	**454**	**416**	**399**	**389**	**385**	**382**
TAVR	**496**	**477**	**469**	**465**	**459**	**453**

PARTNER 3 trial

Primary Endpoint – Subgroup Analysis

Subgroup	TAVR	Surgery	Diff [95% CI]	P-value*
Overall	**8.5**	**15.1**	**-6.6 [-10.8, -2.5]**	
Age				
≤ 74 (n=516)	10.6	14.9	-4.3 [-10.1, 1.5]	**0.21**
> 74 (n=434)	5.8	15.3	-9.5 [-15.3, -3.7]	
Sex				
Female (n=292)	8.1	18.5	-10.4 [-18.3, -2.5]	**0.27**
Male (n=658)	8.7	13.8	-5.1 [-9.9, -0.3]	
STS Score				
≤ 1.8 (n=464)	9.1	15.7	-6.7 [-12.6, -0.7]	**0.98**
> 1.8 (n=486)	8.0	14.5	-6.5 [-12.2, -0.8]	
LV Ejection Fraction				
≤ 65 (n=384)	9.6	17.2	-7.6 [-14.5, -0.7]	**0.48**
> 65 (n=524)	8.0	12.4	-4.4 [-9.6, 0.7]	
NYHA Class				
I/II (n=687)	6.8	14.5	-7.8 [-12.4, -3.2]	**0.54**
III/IV (n=263)	12.3	16.9	-4.7 [-13.5, 4.1]	
Atrial Fibrillation				
No (n=786)	7.9	14.0	-6.1 [-10.5, -1.7]	**0.67**
Yes (n=163)	11.6	20.3	-8.7 [-19.9, 2.5]	
KCCQ Overall Summary Score				
≤ 70 (n=407)	10.5	19.9	-9.4 [-16.5, -2.4]	**0.27**
> 70 (n=536)	6.5	11.2	-4.6 [-9.4, 0.2]	



Event rates are KM estimates (%)

* P-value is for interaction

PARTNER 3 trial

Pre-specified Secondary Endpoints

Subject to Multiplicity Adjustment

Order of Testing	Endpoint	TAVR (N=496)	Surgery (N=454)	Treatment Effect [95% CI]	P-value
1	New onset atrial fibrillation at 30 days	5.0%	39.5%	0.10 [0.06, 0.16]	<0.001
2	Length of index hospitalization (days)	3.0 (2.0, 3.0)	7.0 (6.0, 8.0)	-4.0 [-4.0, -3.0]	<0.001
3	All-cause death, all stroke, or rehospitalizations at 1 year	8.5%	15.1%	0.54 [0.37, 0.79]	0.001
4	Death, KCCQ < 45 or KCCQ decrease from baseline ≥ 10 points at 30 days	3.9%	30.6%	-26.7% [-31.4%, -22.1%]	<0.001
5	Death or all stroke at 30 days	1.0%	3.3%	0.30 [0.11, 0.83]	0.01
6	All stroke at 30 days	0.6%	2.4%	0.25 [0.07, 0.88]	0.02

* P-value is Log-Rank test for items 1, 3, 5 and 6; P-value is Wilcoxon Rank-Sum Test for item 2; P-value is Fisher's Exact test for item 4

PARTNER 3 trial

Other Secondary Endpoints

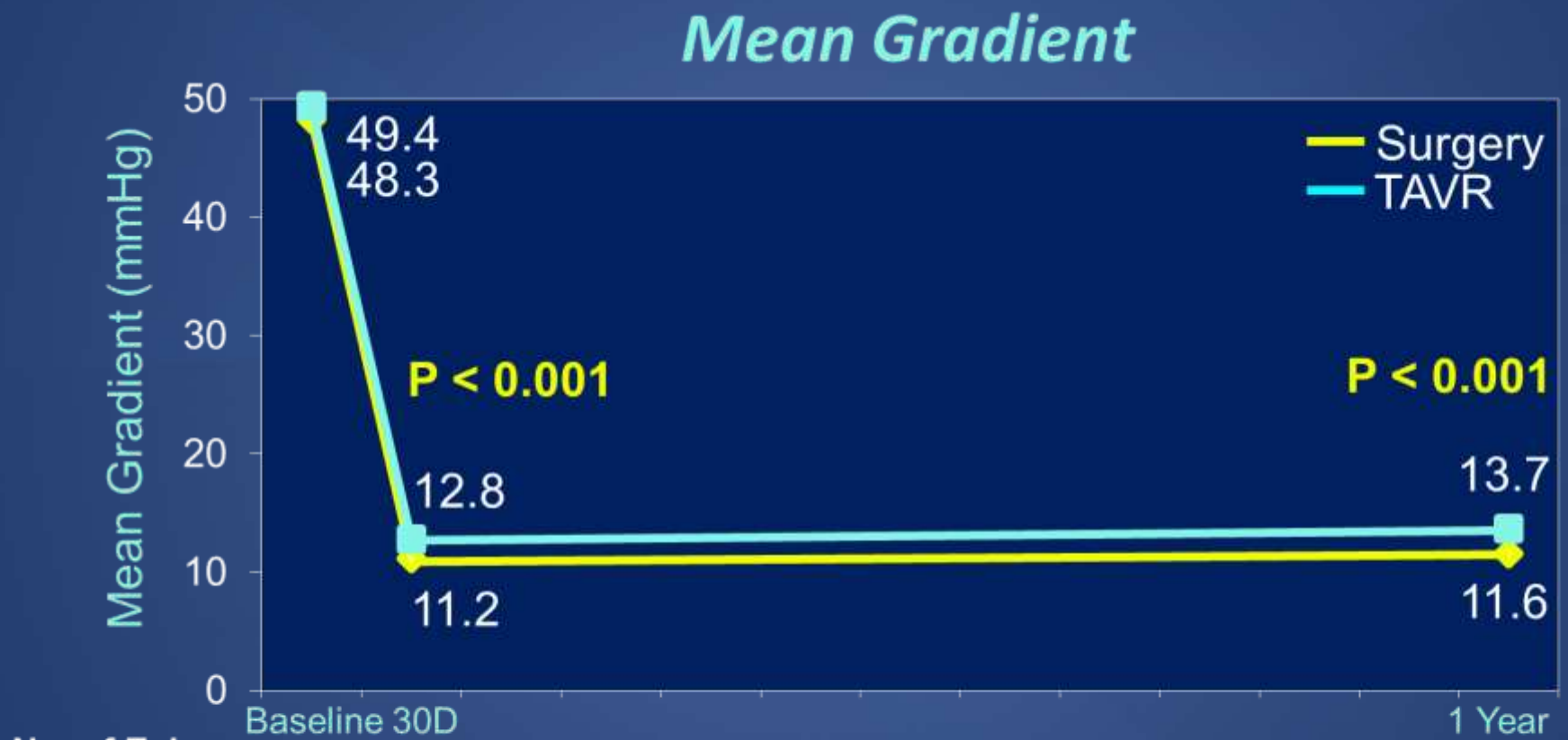
Outcomes	30 Days			1 Year		
	TAVR (N=496)	Surgery (N=454)	P-value	TAVR (N=496)	Surgery (N=454)	P-value
Bleeding - Life-threat/Major	3.6% (18)	24.5% (111)	<0.001	7.7% (38)	25.9% (117)	<0.001
Major Vascular Complics	2.2% (11)	1.5% (7)	0.45	2.8% (14)	1.5% (7)	0.19
AKI - stage 2 or 3*	0.4% (2)	1.8% (8)	0.05	0.4% (2)	1.8% (8)	0.05
New PPM (incl baseline)	6.5% (32)	4.0% (18)	0.09	7.3% (36)	5.4% (24)	0.21
New LBBB	22.0% (106)	8.0% (35)	<0.001	23.7% (114)	8.0% (35)	<0.001
Coronary Obstruction	0.2% (1)	0.7% (3)	0.28	0.2% (1)	0.7% (3)	0.28
AV Re-intervention	0% (0)	0% (0)	NA	0.6% (3)	0.5% (2)	0.76
Endocarditis	0% (0)	0.2% (1)	0.29	0.2% (1)	0.5% (2)	0.49
Asymp Valve Thrombosis	0.2% (1)	0% (0)	0.34	1.0% (5)	0.2% (1)	0.13

Event rates are KM estimates (%) and p-values are based on Log-Rank test

* Event rates are incidence rates and p-value is Fisher's Exact test

PARTNER 3 trial

Echocardiography Findings



No. of Echos			
Surgery	441	426	390
TAVR	483	490	469

P-values are based on the ANCOVA for TAVR vs Surgery adjusted by baseline.

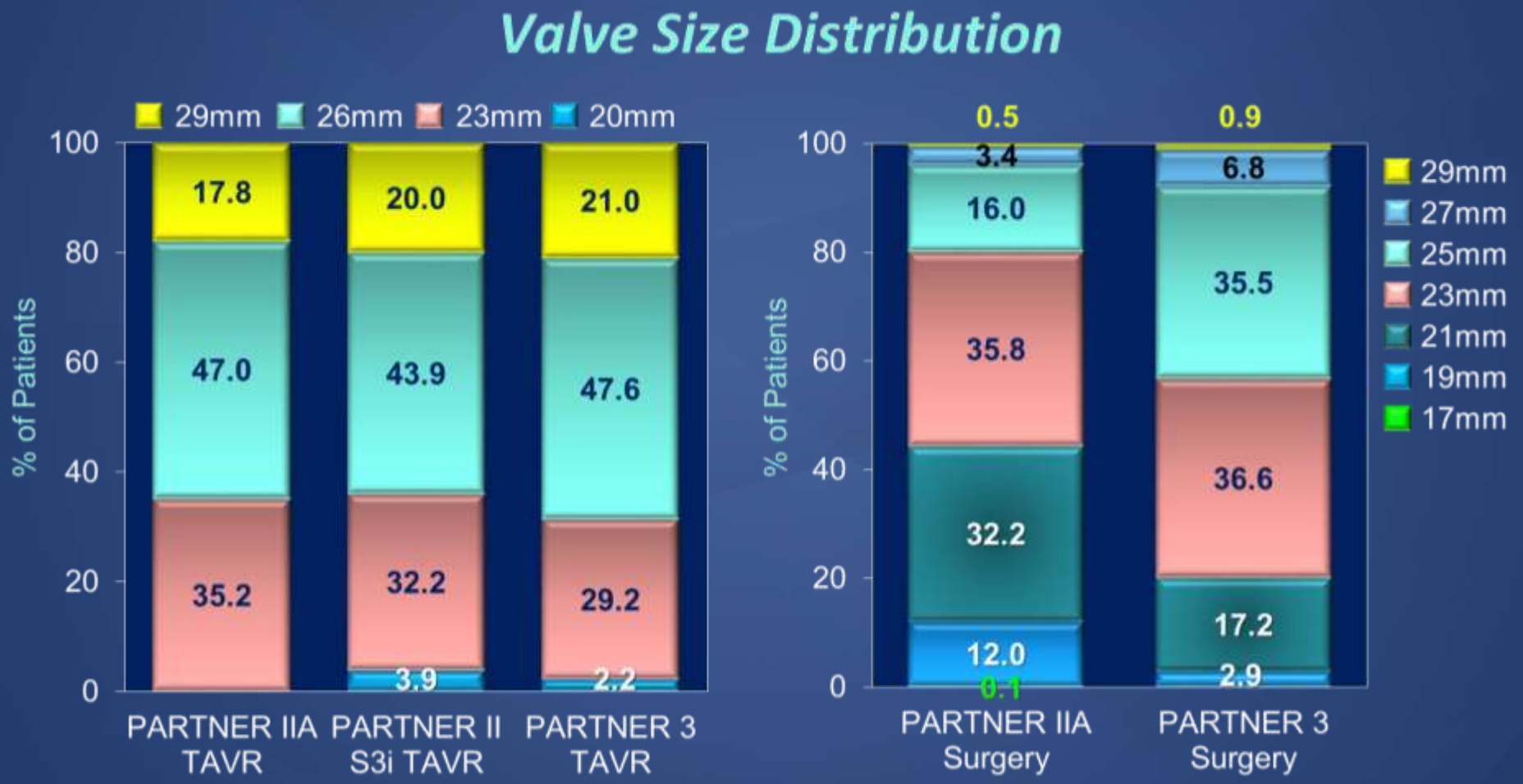
PARTNER 3 trial

Echocardiography Findings

No. of Echos			
Surgery	423	395	371
TAVR	458	470	446

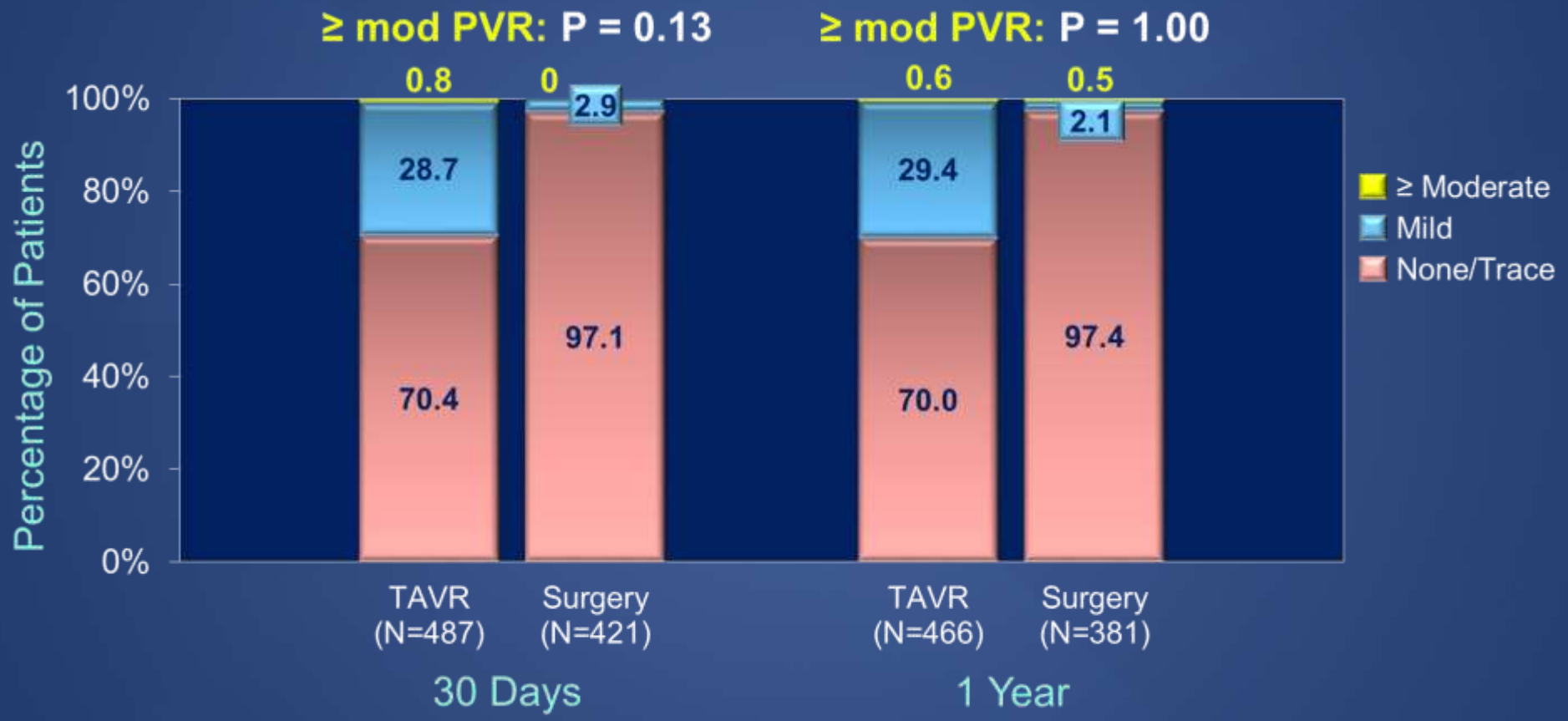
P-values are based on the ANCOVA for TAVR vs Surgery adjusted by baseline.

The PARTNER trials



PARTNER 3 trial

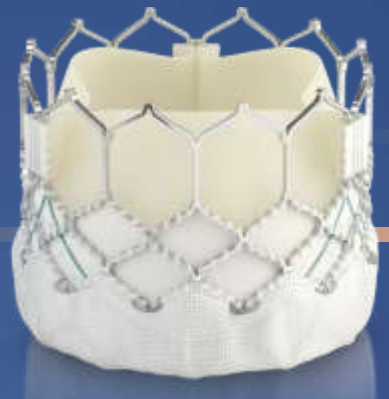
Paravalvular Regurgitation



P-values are based on the Wilcoxon rank-sum test.

SAPIEN 3 Ultra

Changes in Sapien Series



Ask

Save lives, starting with the sickest patients

Extend life-saving treatment to even more

Reset the bar to be superior to surgery

Continue to meet the emerging needs of new patient populations

2007

- EU Approval
- Start of PARTNER trial

2011 Kr

2016 Apr

2022 2wk Jul

Response

SAPIEN valve
Introducing TAVI as a life-saving treatment option for patients that are inoperable or high-risk for surgery[1]

SAPIEN XT valve
Non inferior to surgery on mortality and stroke in intermediate risk patients[2]

SAPIEN 3 valve
The only THV proven superior to surgery for low risk patients[3]

SAPIEN 3 Ultra valve
Further reducing PVL, reaching new patients with expanded indications[4]

2019 FDA

1. Leon MB, Smith CR, Mack MJ, et al. Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery. N Engl J Med. 2010.
2. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients. N Engl J Med. 2016.
3. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients. N Engl J Med. 2019.
4. Nazif T, Daniels D, McCabe J, Chehab B, et al. Real-world experience with the SAPIEN 3 Ultra TAVI: A propensity matched analysis from the United States. Presented virtually at TVT Connect 2020.

Edwards SAPIEN 3 Ultra System

: Complete range of valve sizes

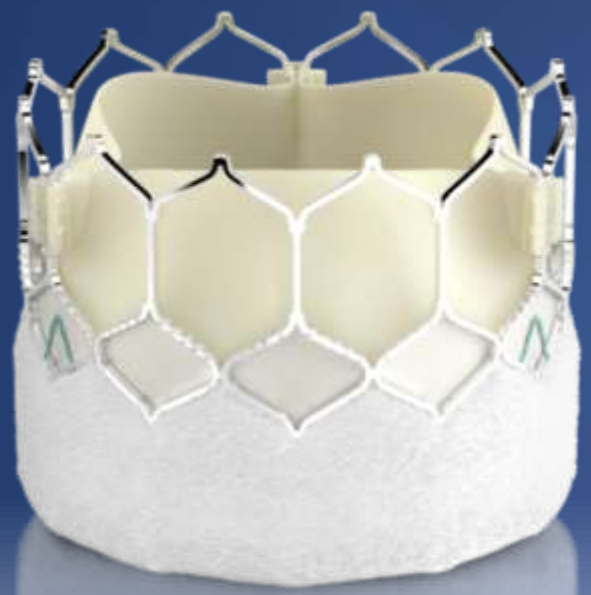
SAPEIN 3 Ultra

	20 mm	23 mm	26 mm	29 mm
Valve	**SAPIEN 3 Ultra**	**SAPIEN 3 Ultra**	**SAPIEN 3 Ultra**	SAPIEN 3
Native Annulus Size by TEE*	16 – 19 mm	18 – 22 mm	21 – 25 mm	24 – 28 mm
Native Annulus Area (CT)*	273 – 345 mm^2	338 – 430 mm^2	430 – 546 mm^2	540 – 683 mm^2
Area-derived Diameter (CT)*	18.6 – 21 mm	20.7 – 23.4 mm	23.4 – 26.4 mm	26.2 – 29.5 mm
Edwards eSheath Introducer set	14F	14F	14F	16F
Minimum access vessel diameter	5.5 mm	5.5 mm	5.5 mm	6.5 mm

**Unchanged between SAPIEN 3 and SAPIEN 3 Ultra valve*

CT, computed tomography; TEE, Transesophageal echocardiogram

Edwards SAPIEN 3 Ultra System



SAPIEN 3 Ultra valve[1]

Featuring a **taller, textured PET** outer skirt[2]

Commander delivery system

Physician controlled dual articulation with tapered distal tip

eSheath set

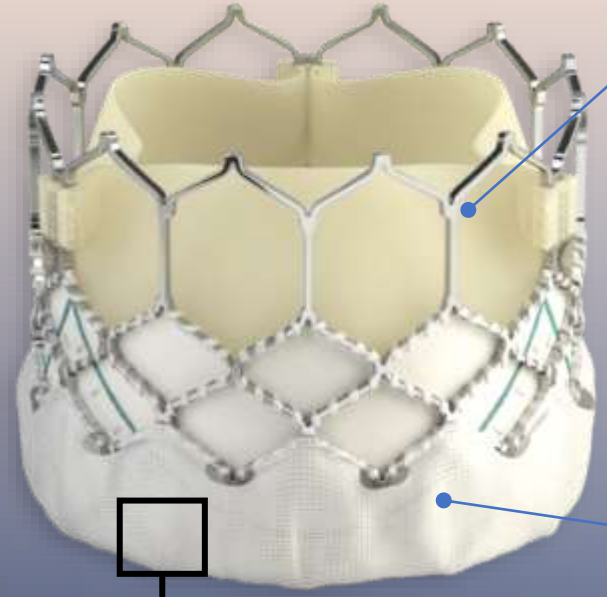
14Fr eSheath compatible

1 Available in 20, 23 and 26mm sizes
2 Compared to the Edwards SAPIEN 3 valve

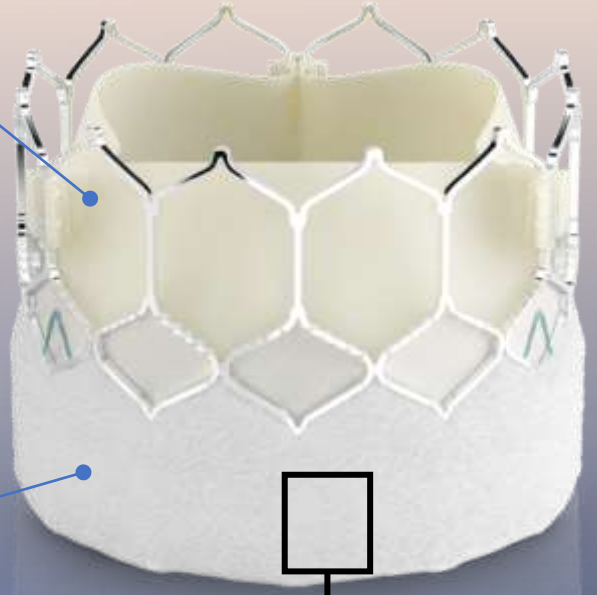
SAPIEN 3 Ultra valve vs SAPIEN 3

Building on the standard in TAVI to meet the needs of today

SAPIEN 3



SAPIEN 3 Ultra



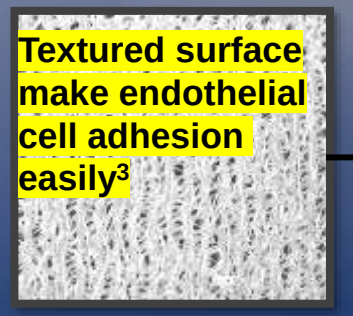
Same frame and leaflet design[1]

- Cobalt-Chrome alloy frame
- Bovine pericardial leaflets
- Cell frame design
- PET outer skirt
- 14F sheath compatibility[2]

Improved taller, textured outer skirt

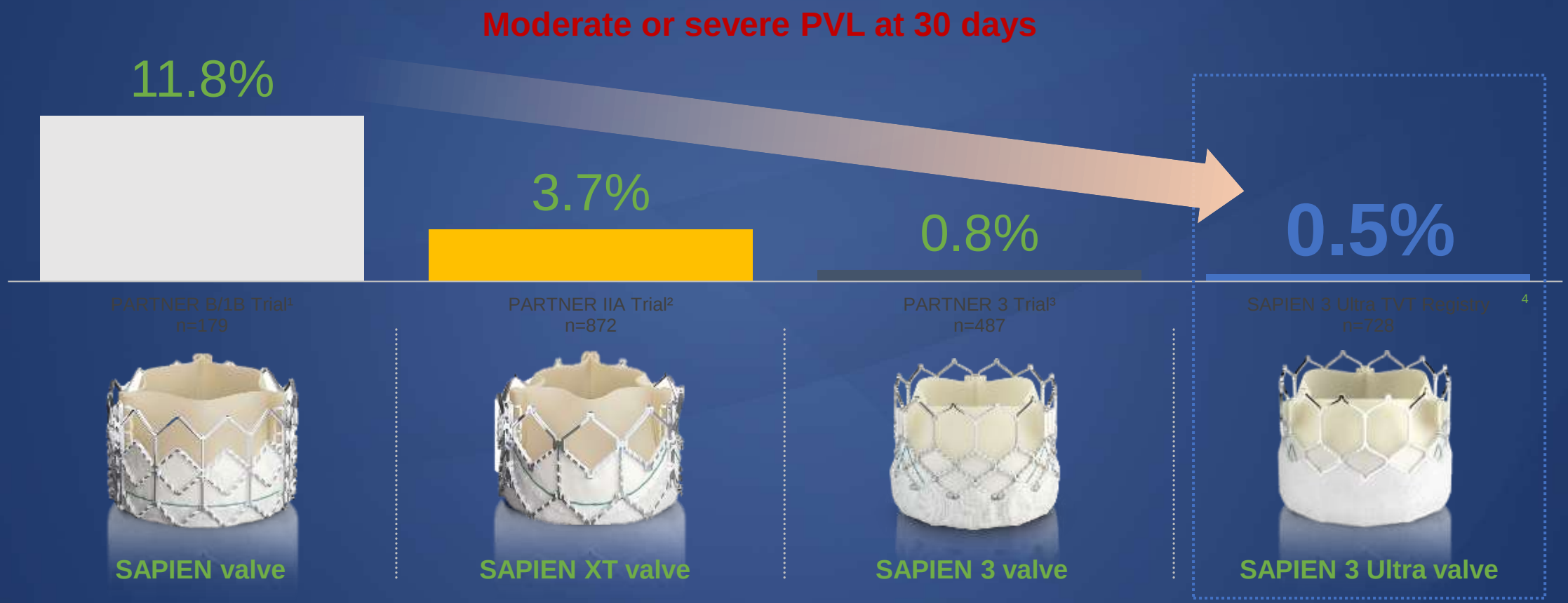
- Approximately 40% increased outer skirt height[1]
- Textured PET (↔ S3 = Flat layered)

  : Enhance healing and endothelialization[3,4]



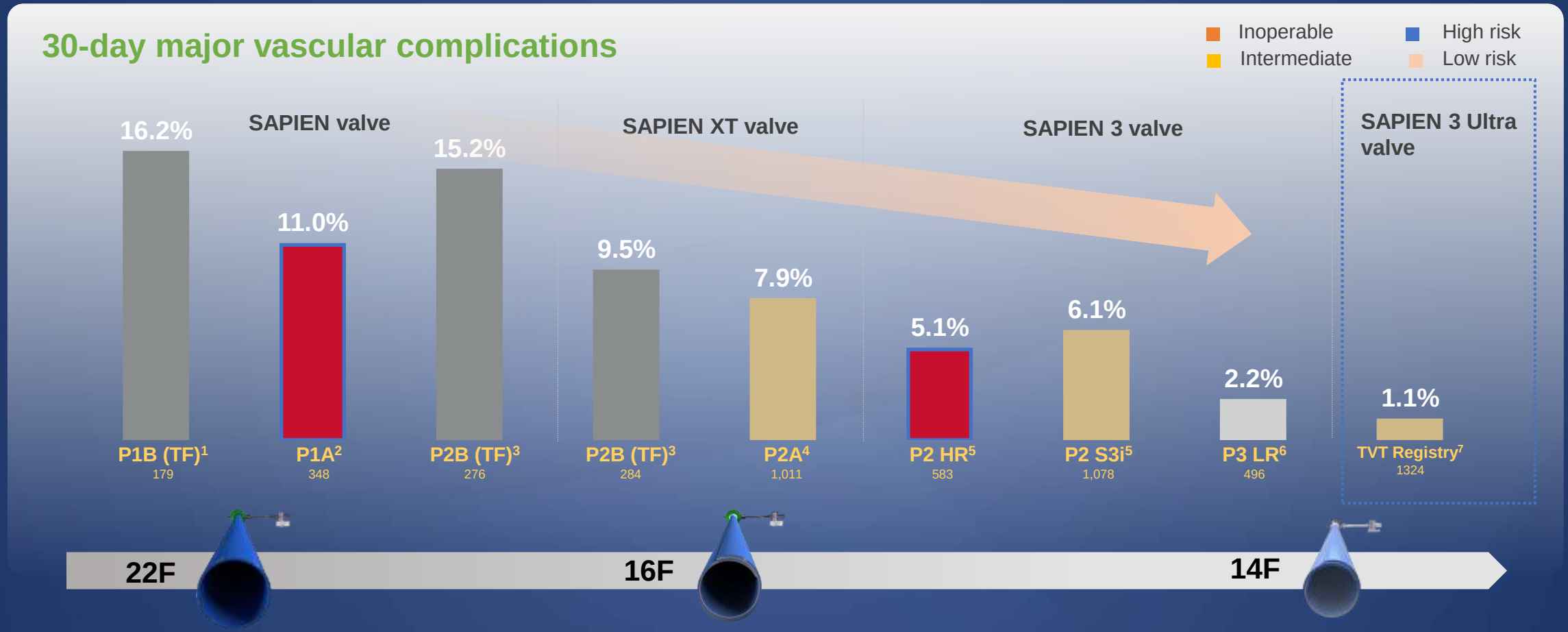
1. Compared to the Edwards SAPIEN 3 valve 2. 2019 4 Ultra transcatheter Aortic Valve Device 3. For 20, 23, and 26 mm sizes 3. Soumen Jana, Acta biomater, 4. Barbanti & Costa, JACC 2020 SAPIEN

Decreased Significant PVL



1. Leon MB, Smith CR, Mack MJ, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med.* 2010;363(17):1597-1607.
2. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med.* 2016;374(17):1609-1620.
3. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med. 2019;380(18):1695-1705.
4. Nazif T, Daniels D, McCabe J, Chehab B, et al. Real-world experience with the SAPIEN 3 Ultra TAVI: A propensity matched analysis from the United States. Presented virtually at TVT Connect 2020.

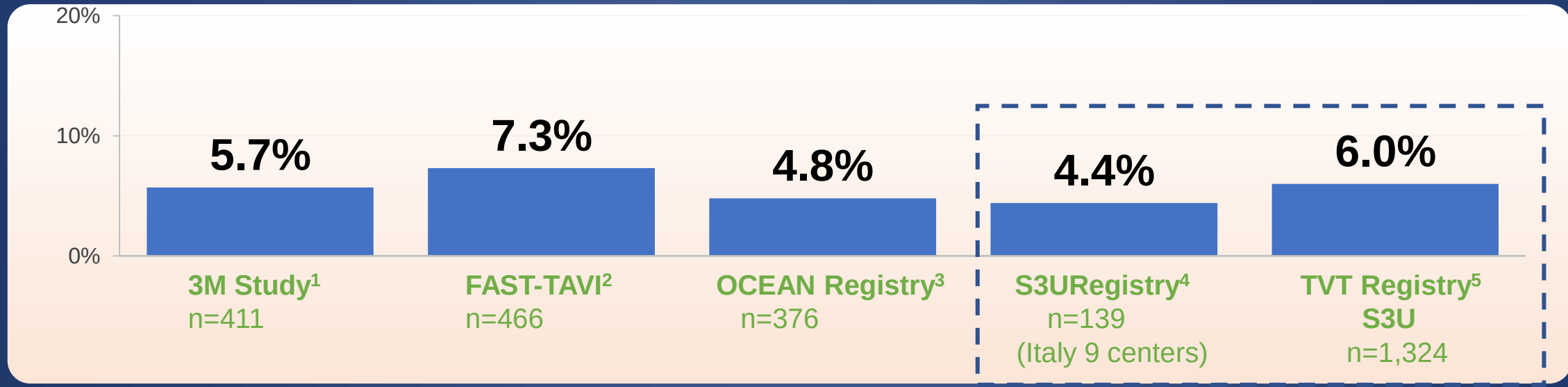
Reduced vascular complications with low profile introducer



1. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med*. 2010;363(17):1597-1607.
2. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus Surgical Aortic-Valve Replacement in High-Risk Patients. *N Engl J Med*. 2011;364:2187-2198.
3. Webb JG, Doshi D, Mack MJ, et al. A randomized evaluation of the SAPIEN XT transcatheter heart valve system in patients with aortic stenosis who are not candidates for surgery. *JACC Cardiovasc Interv*. 2015;8(14):1797-1806.
4. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med*. 2016;374:1609-1620.
5. Kodali S, Thourani VH, White J, et al. Early clinical and echocardiographic outcomes after SAPIEN 3 transcatheter aortic valve replacement in inoperable, high-risk and intermediate-risk patients with aortic stenosis. *Eur Heart J*. 2016;37(28):2252-2262.
6. Mack M, Leon M, Thourani R, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med 2019;380:1695-705.
7. Nazif T, Daniels D, McCabe J, Chehab B, et al. Real-world experience with the SAPIEN 3 Ultra TAVI: A propensity matched analysis from the United States. Presented virtually at TVT Connect 2020

Predictability and control, to further reduce the risk of conduction disturbances with SAPIEN 3 Ultra

Globally consistent, single-digit new permanent pacemaker rates



1. Wood, DA, Lauck SB, Cairns JA, et al. The Vancouver 3M (multidisciplinary, multimodality, but minimalist) clinical pathway facilitates safe next-day discharge home at low-, medium-, and high-volume transfemoral transcatheter aortic valve replacement centers: the 3M TAVI study. *J Am Coll Cardiol Intv.* 2019;12(5):459-469.
2. Barbanti M, van Mourik MS, Spence MS, et al. Optimising patient discharge management after transfemoral transcatheter aortic valve implantation: the multicentre European FAST-TAVI trial. *EuroIntervention.* 2019;15:147-154.
3. Yamamoto M, Watanabe Y, Tada N, et al. Transcatheter aortic valve replacement outcomes in Japan: optimized catheter valvular intervention (OCEAN) Japanese multicenter registry. *Cardiovasc Revasc Med.* 2019;20(10):843-851.
4. Saia F, et al. In-hospital and thirty day outcomes of the SAPIEN 3 Ultra balloon-expandable TAVR: the S3U registry. Eurointervention 2020.
5. Nazif T, Daniels D, McCabe J, Chehab B, et al. Real-world experience with the SAPIEN 3 Ultra TAVR: A propensity matched analysis from the United States. Presented virtually at TVT Connect 2020.

SAPIEN 3 Ultra Outcomes in TVT Registry

Delivering outcomes your patients can count on:

30 days (TVT registry, 2021)

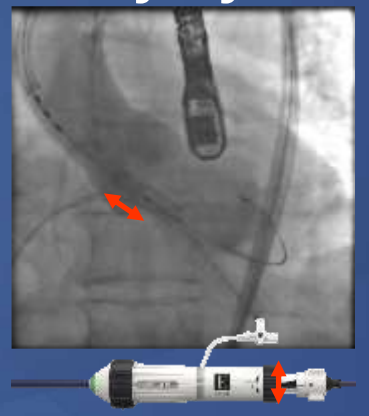
n=1,324	S3U TAVI[1]
All-cause mortality	0.9%
All-cause stroke	1.2%
Rehospitalization	4.4%
New permanent pacemaker	6.0%
Major vascular complication	1.1%
Life-threatening bleeding	0.0%

1. Nazif T, Daniels D, McCabe J, Chehab B, et al. Real-world experience with the SAPIEN 3 Ultra TAVI: A propensity matched analysis from the United States. Presented virtually at TVT Connect 2020

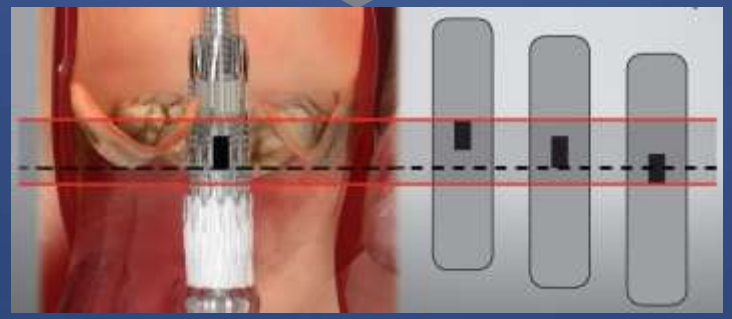
Optimal Initial Valve Positioning Using Fine Control Features of Edward Commander Delivery System

Edwards Commander Delivery System

Dual Articulation

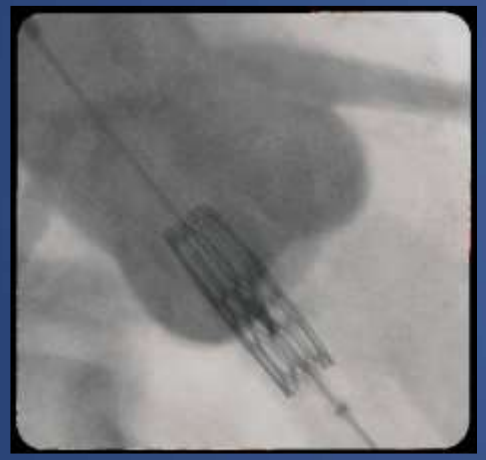
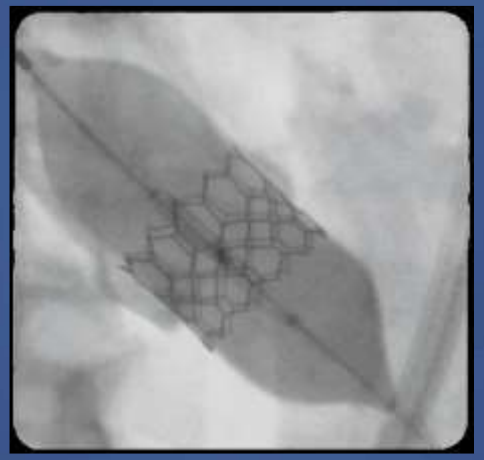


Fine Positioning



Optimal Center Marker Zone (6mm)

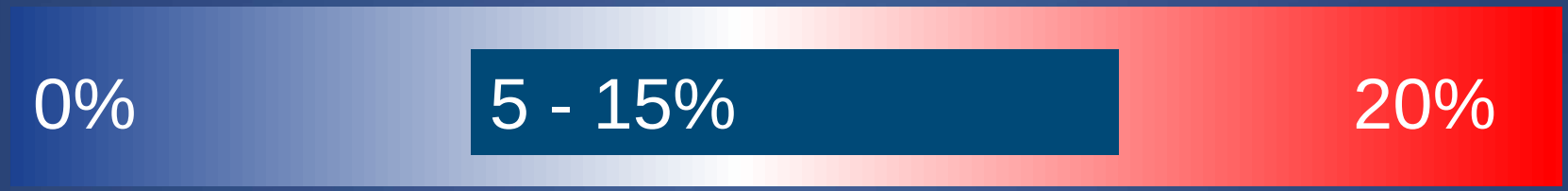
Designed for Precise Deployment and Positioning

Initial Positioning	Deployment	Final placement
		
Use Center Marker and fine positioning feature	Slow, controlled initial inflation using nominal volume	Precise placement

Over 99% of valves placed in the intended location*

* PARTNER II Trial high-risk & inoperable TF SAPIEN 3 valve cohort

Optimal Target for Area Oversizing : SAPIEN 3



Paravalvular leakage

Optimal

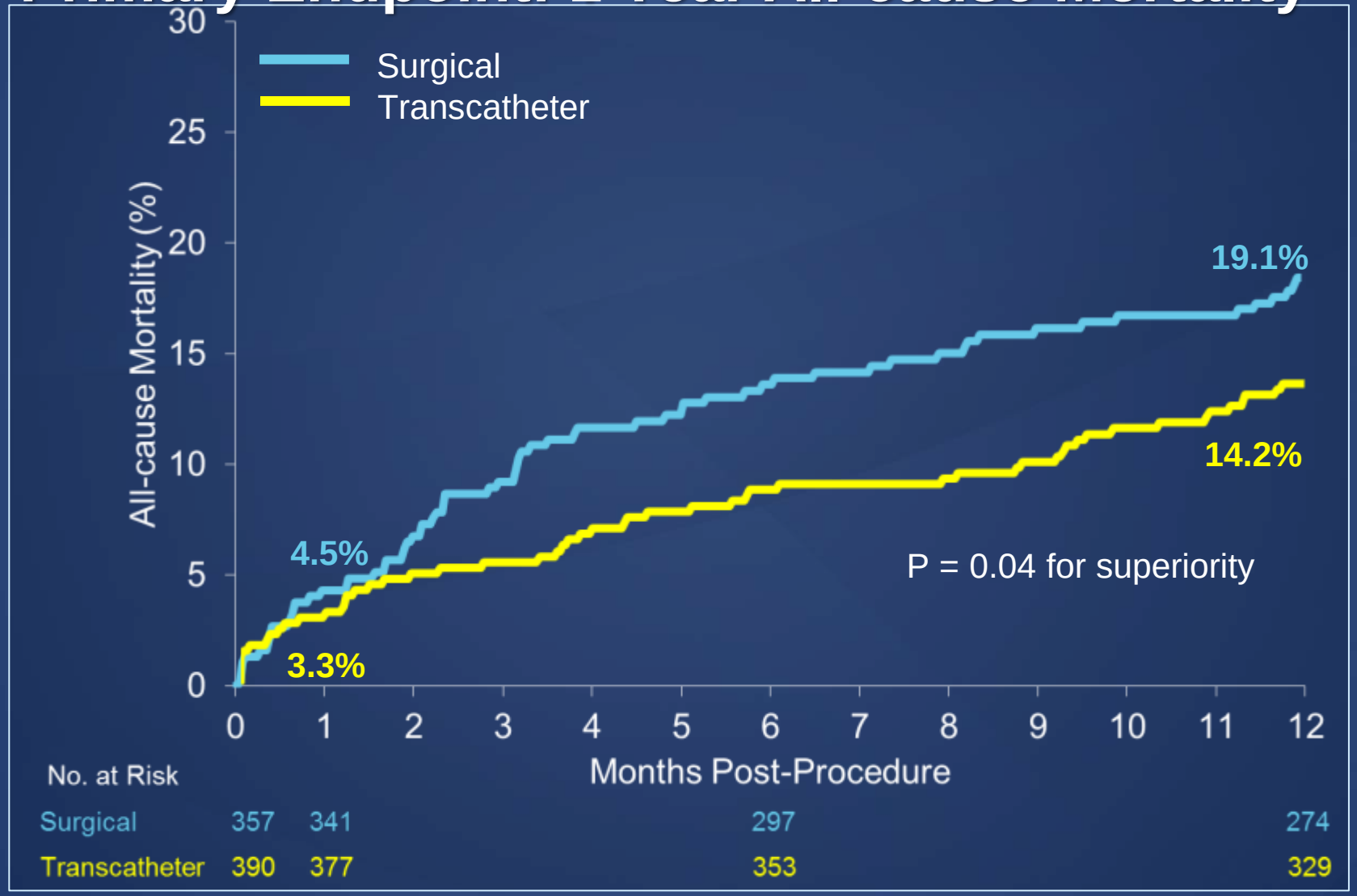
Annulus Rupture

PPM

CoreValve Trials

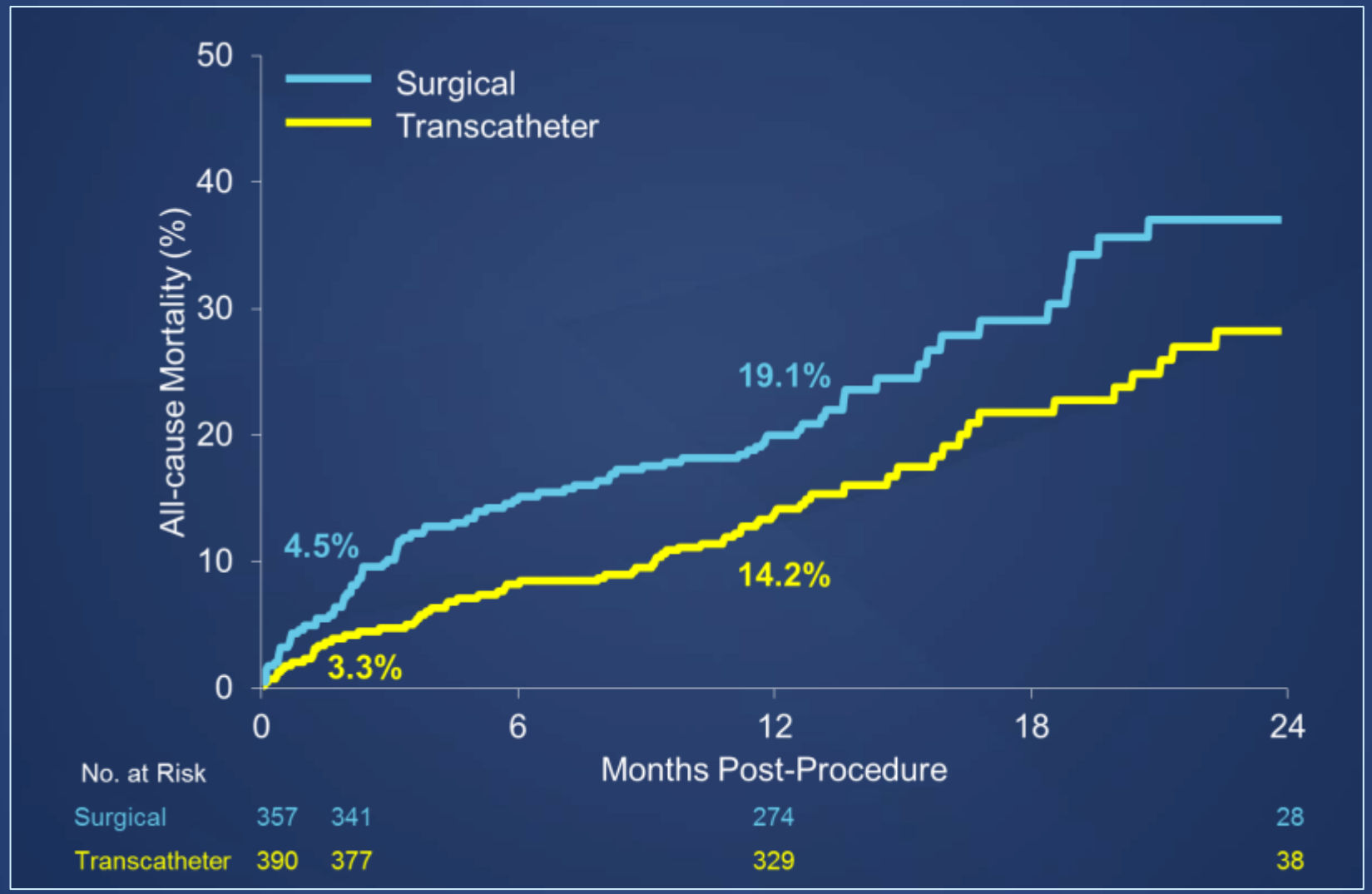
CoreValve US Pivotal Trial

Primary Endpoint: 1 Year All-cause Mortality



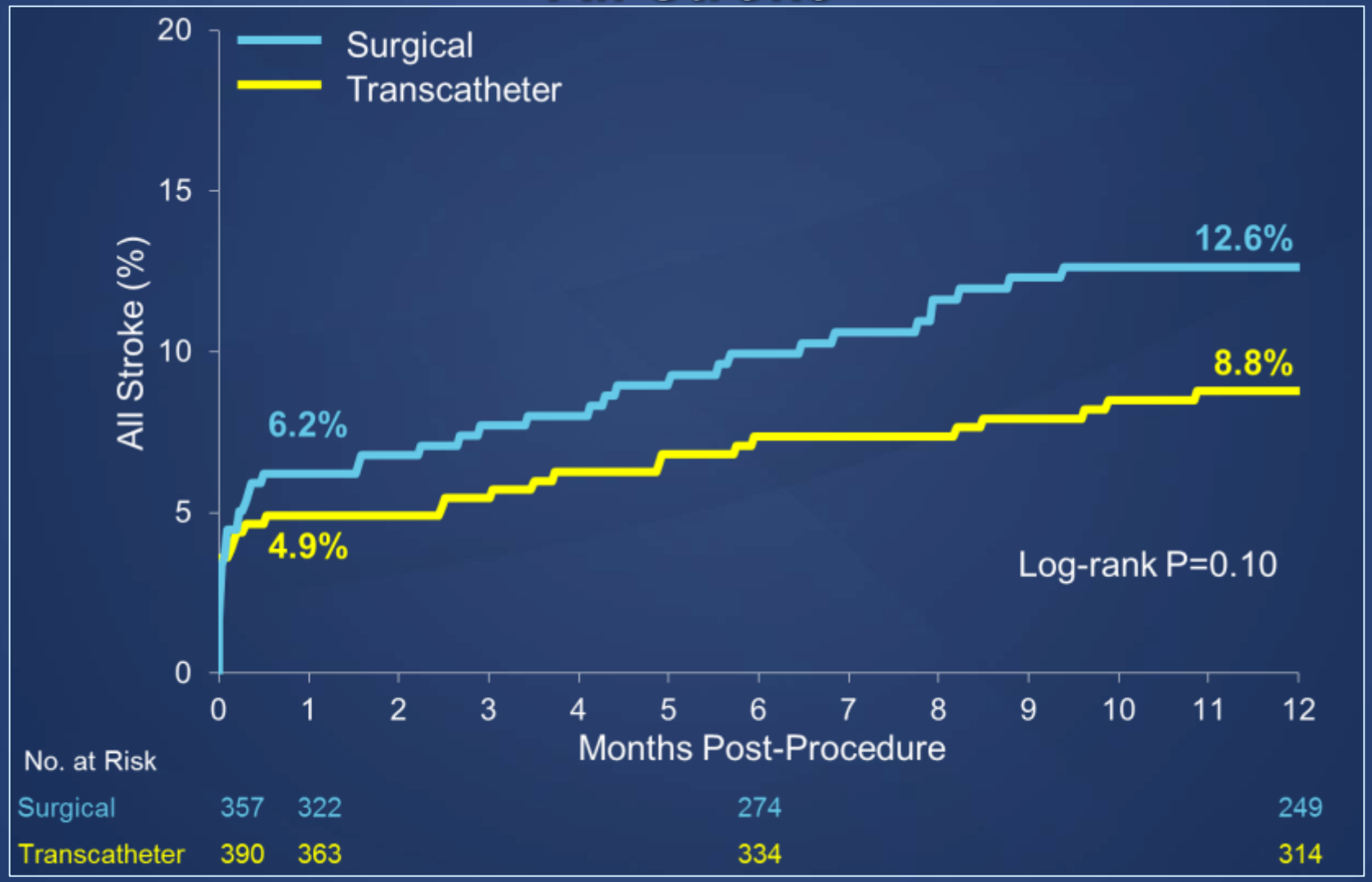
CoreValve US Pivotal Trial

2-Year All-cause Mortality



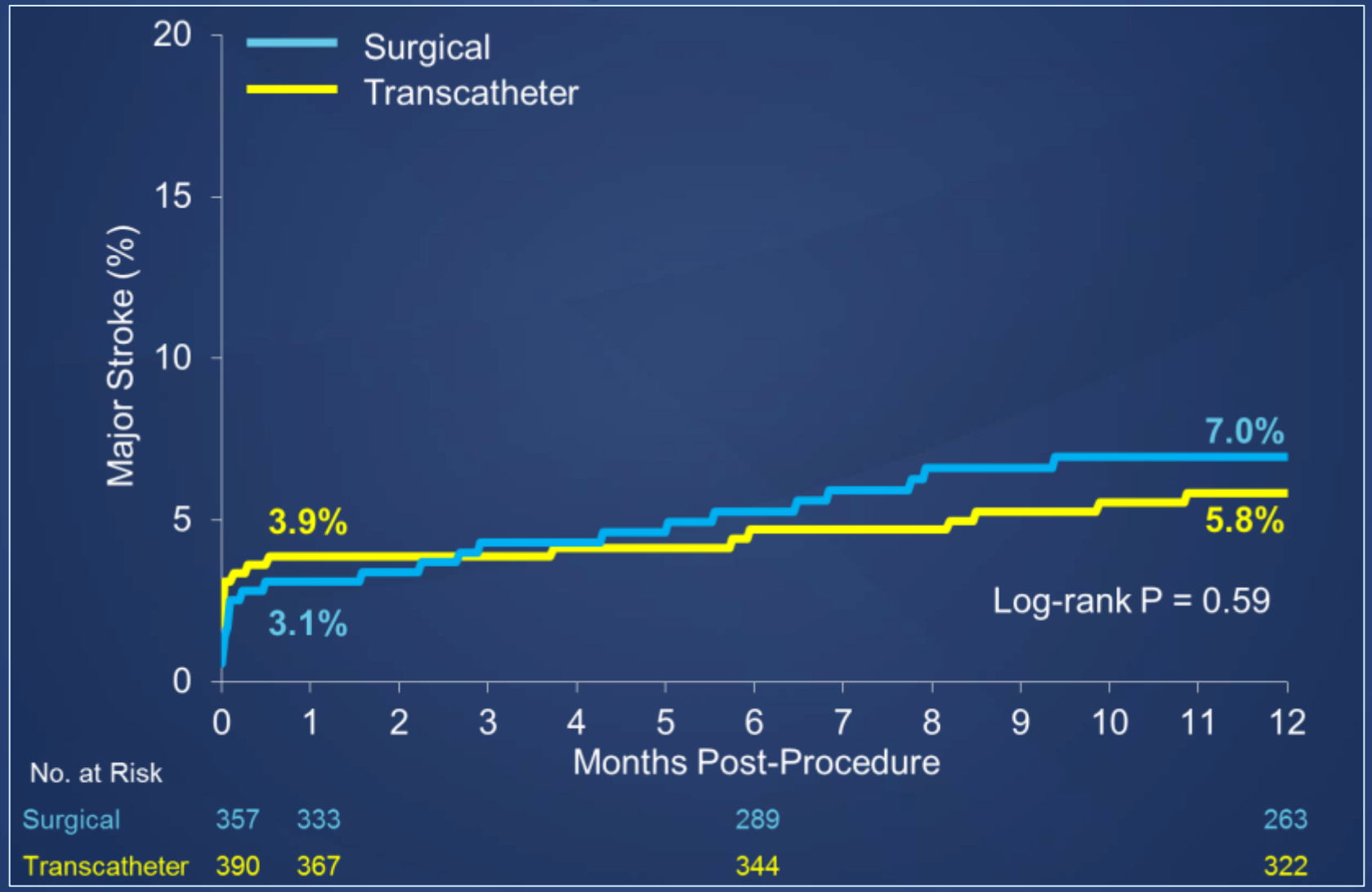
CoreValve US Pivotal Trial

All Stroke



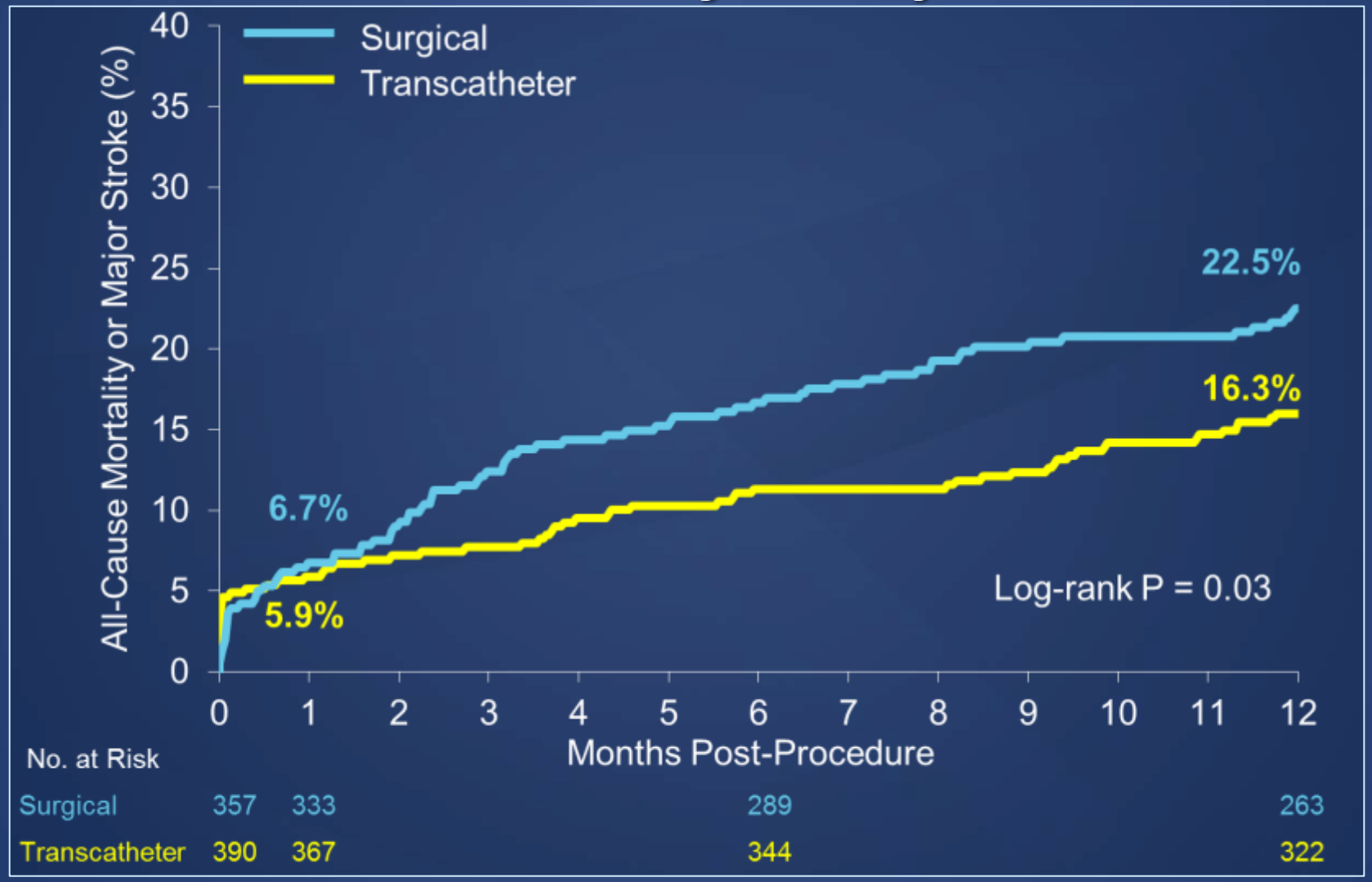
CoreValve US Pivotal Trial

Major Stroke



CoreValve US Pivotal Trial

All-Cause Mortality or Major Stroke



CoreValve US Pivotal Trial

Other Endpoints

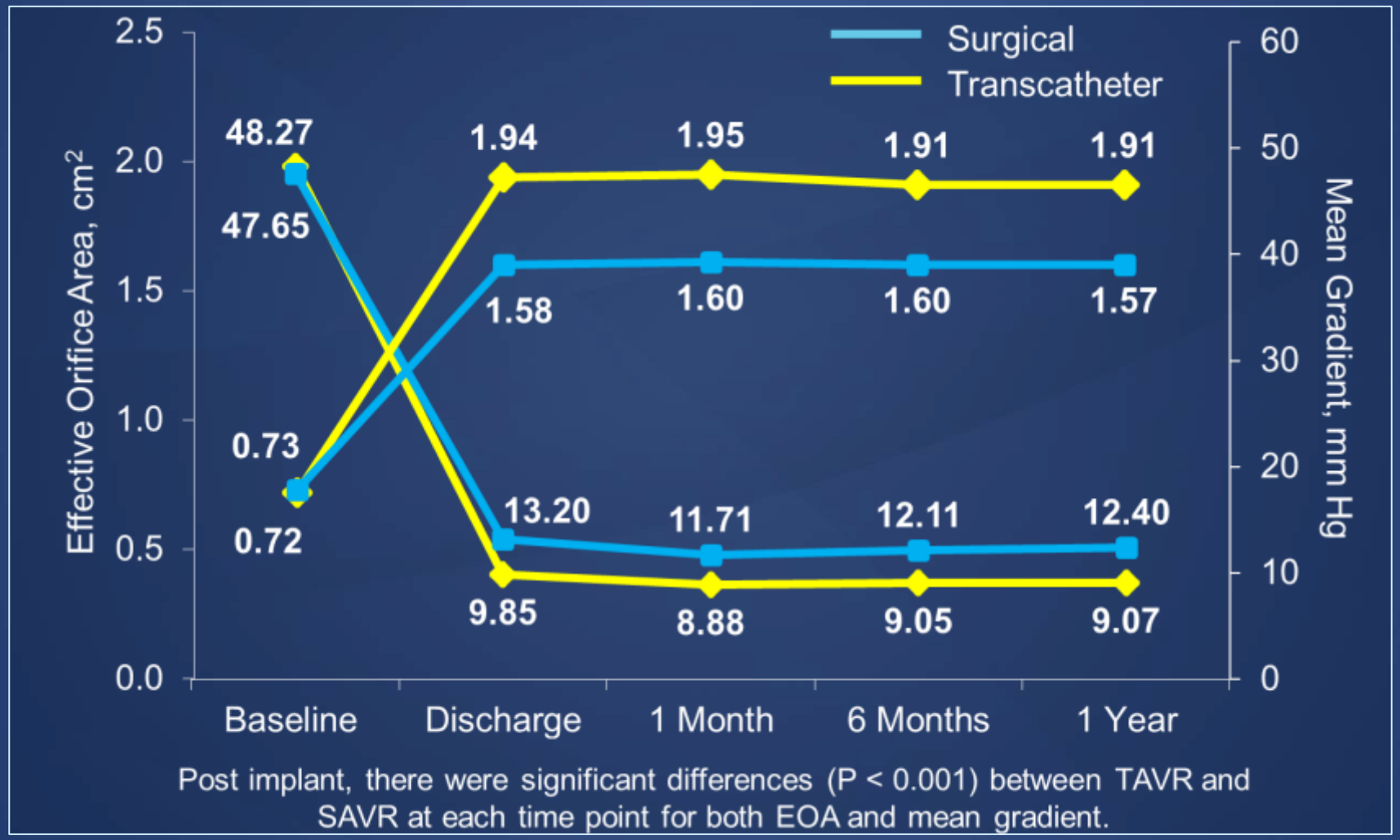
Events*	1 Month			1 Year		
	TAVR	SAVR	P Value	TAVR	SAVR	P Value
Vascular complications (major), %	5.9	1.7	0.003	6.2	2.0	0.004
Pacemaker implant, %	19.8	7.1	<0.001	22.3	11.3	<0.001
Bleeding (life threatening or disabling),%	13.6	35.0	<0.001	16.6	38.4	<0.001
New onset or worsening atrial fibrillation, %	11.7	30.5	<0.001	15.9	32.7	<0.001
Acute kidney injury, %	6.0	15.1	<0.001	6.0	15.1	<0.001

* Percentages reported are Kaplan-Meier estimates and log-rank P values

Adams DH, Popma JJ, Reardon MJ, et al. New Engl J Med 2014; Mar 29, [Epub ahead of print]

CoreValve US Pivotal Trial

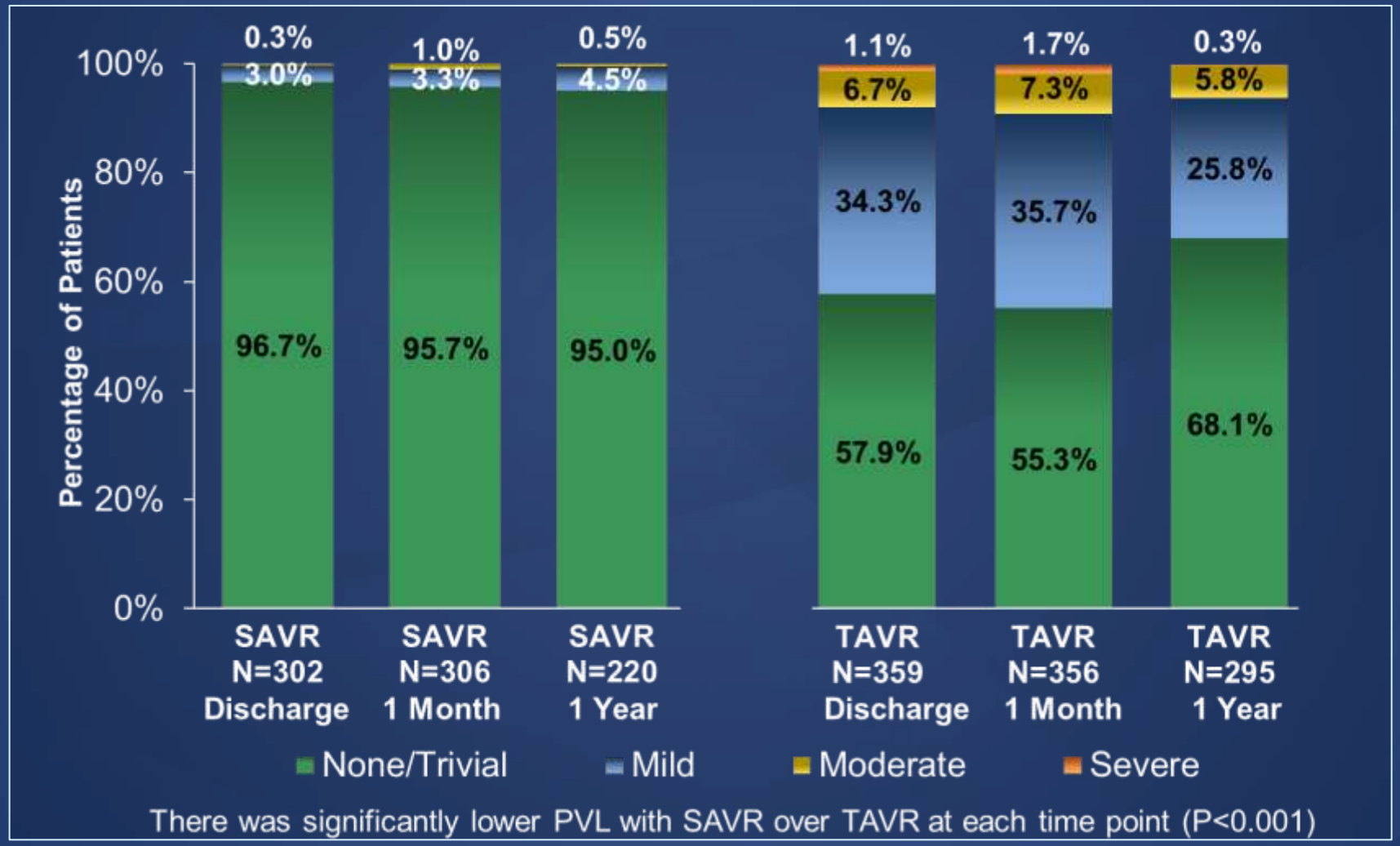
Echocardiographic Findings



Post implant, there were significant differences ($P < 0.001$) between TAVR and SAVR at each time point for both EOA and mean gradient.

CoreValve US Pivotal Trial

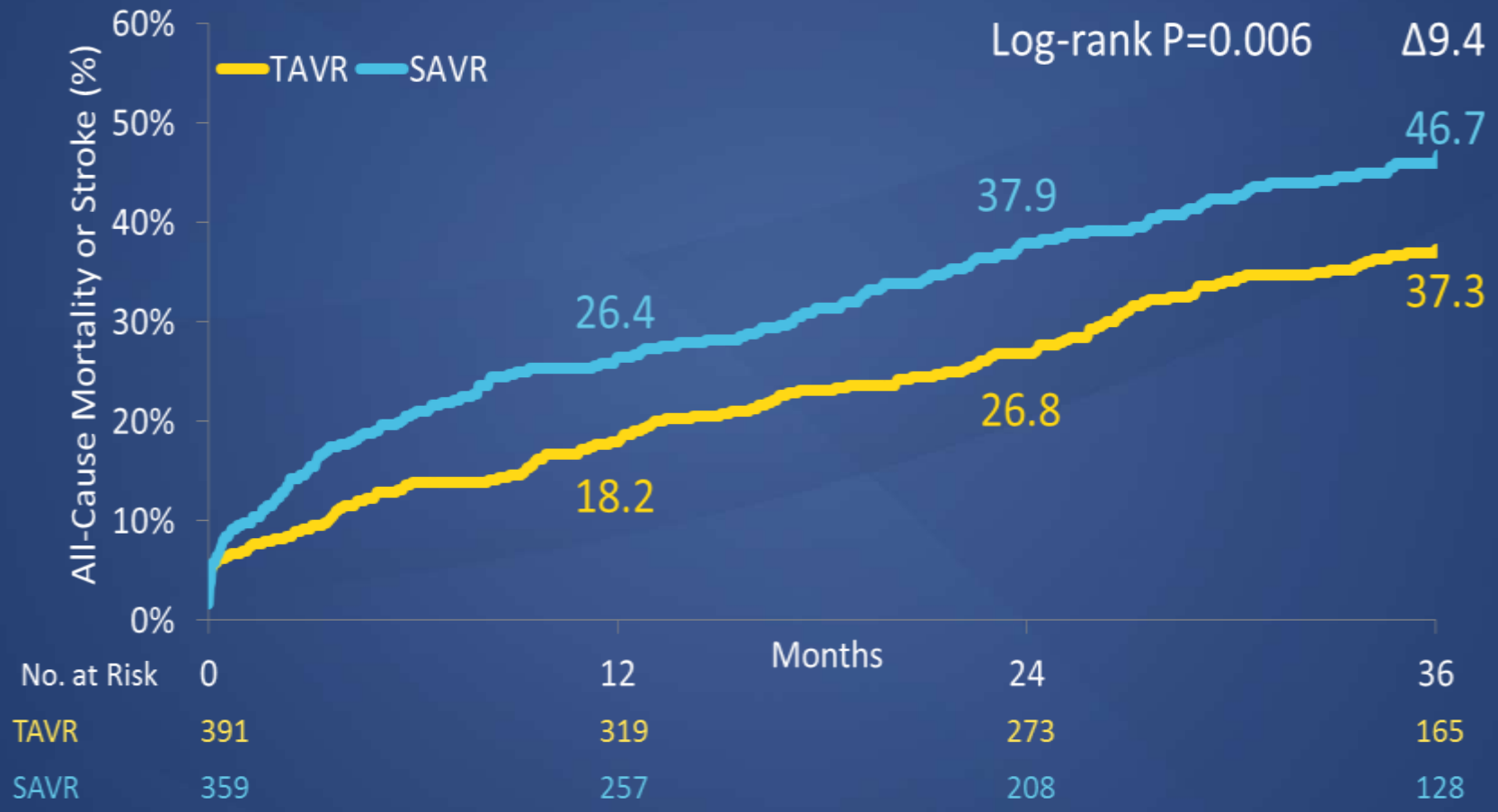
Paravalvular Regurgitation



There was significantly lower PVL with SAVR over TAVR at each time point (P<0.001)

CoreValve US Pivotal Trial– 3 year result

All-Cause Mortality or Stroke



Deeb GM et al. J Am Coll Cardiol. 2016;67(22):2565-74.

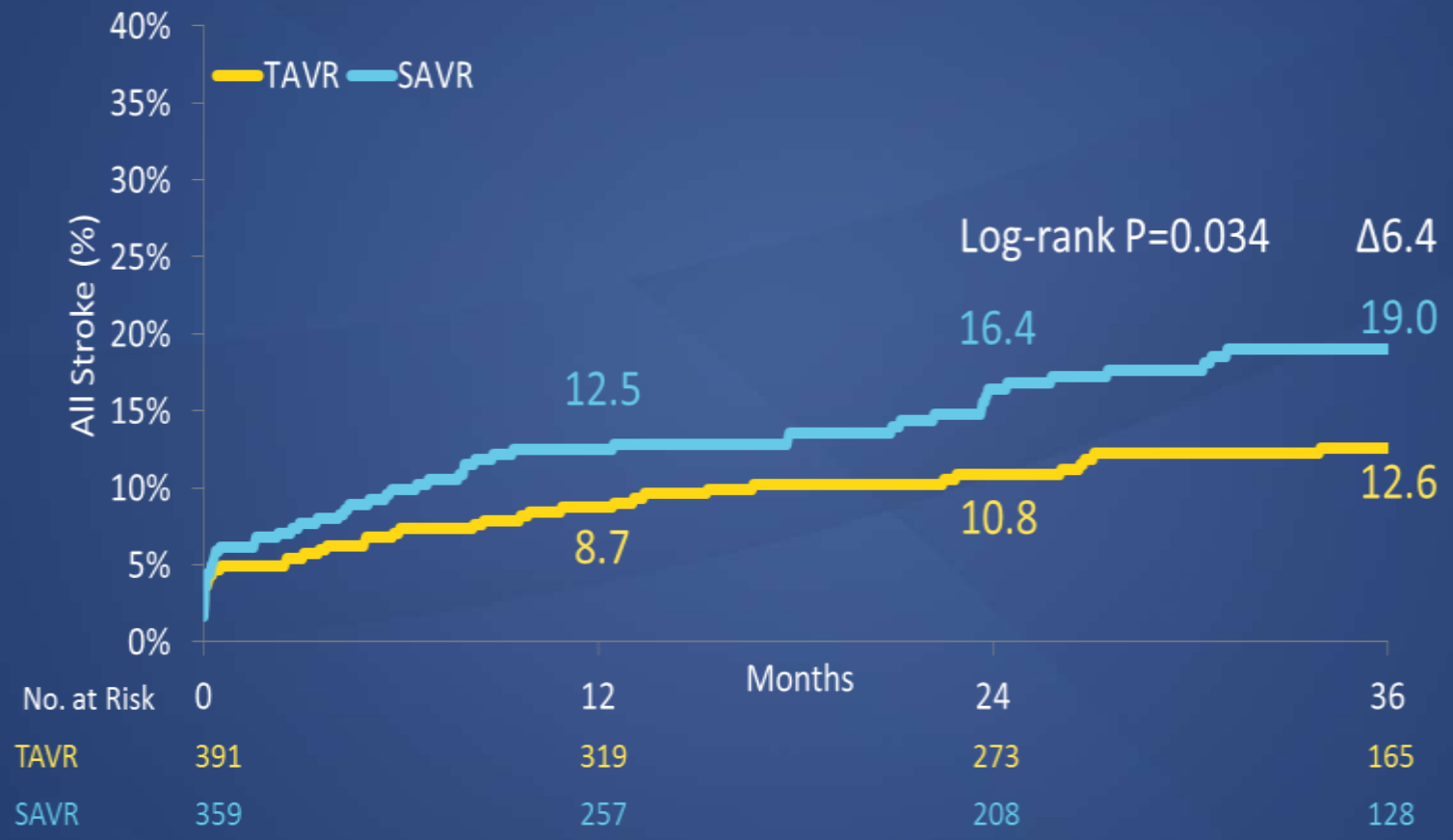
CoreValve US Pivotal Trial– 3 year result

All-Cause Mortality or Major Stroke

Deeb GM et al. J Am Coll Cardiol. 2016;67(22):2565-74.

CoreValve US Pivotal Trial– 3 year result

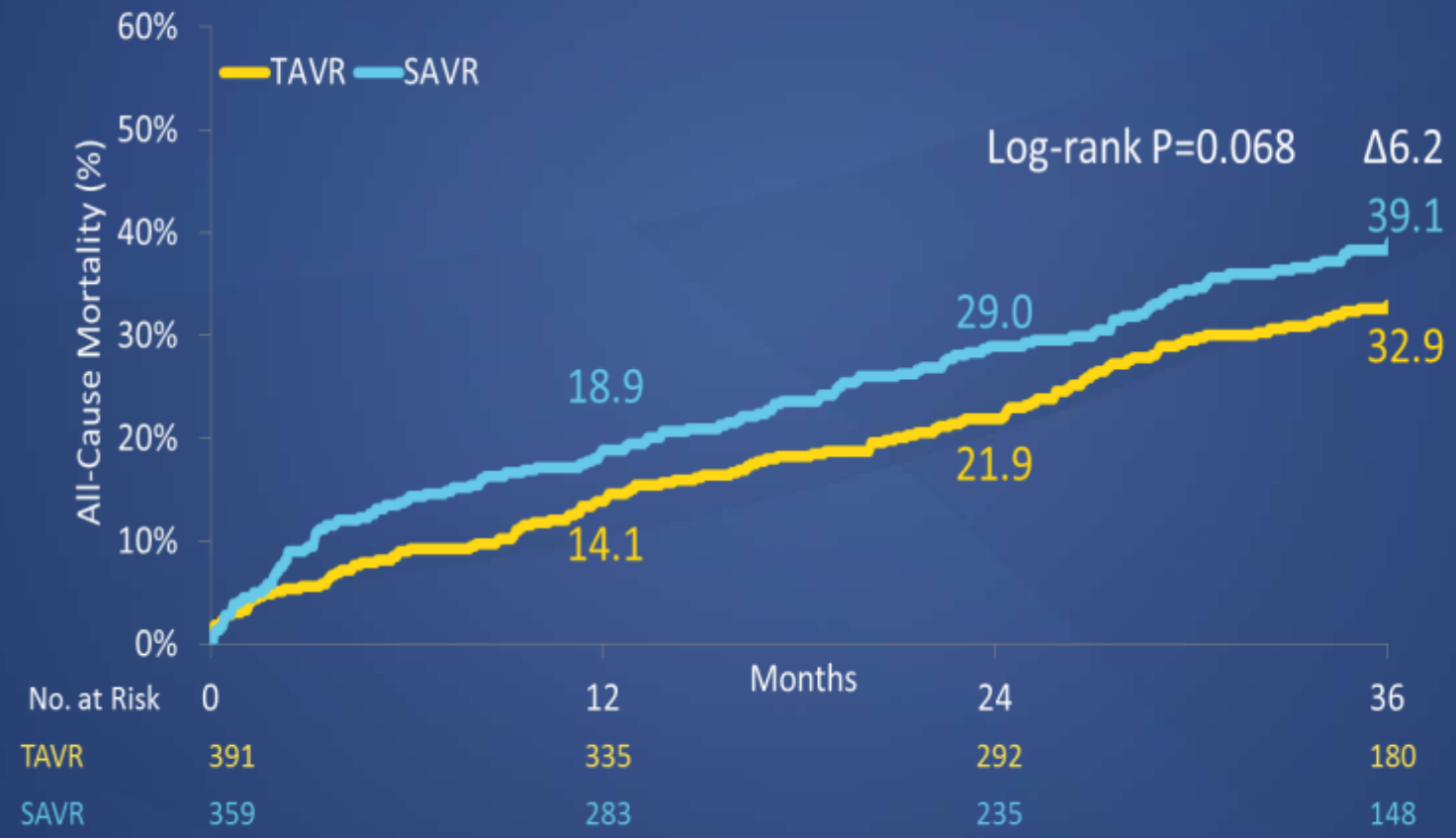
All Stroke



Deeb GM et al. J Am Coll Cardiol. 2016;67(22):2565-74.

CoreValve US Pivotal Trial– 3 year result

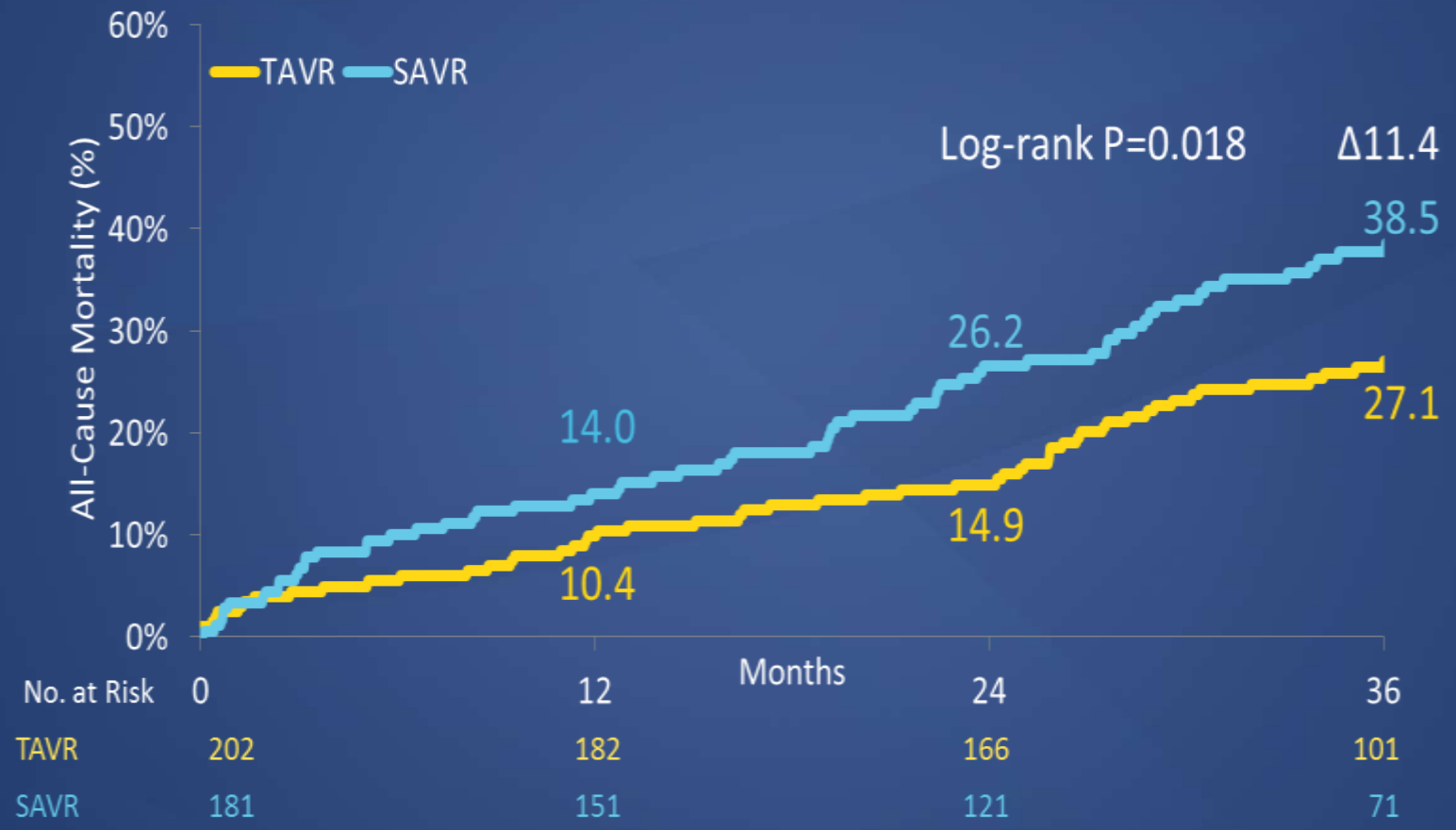
All-Cause Mortality



Deeb GM et al. J Am Coll Cardiol. 2016;67(22):2565-74.

CoreValve US Pivotal Trial– 3 year result

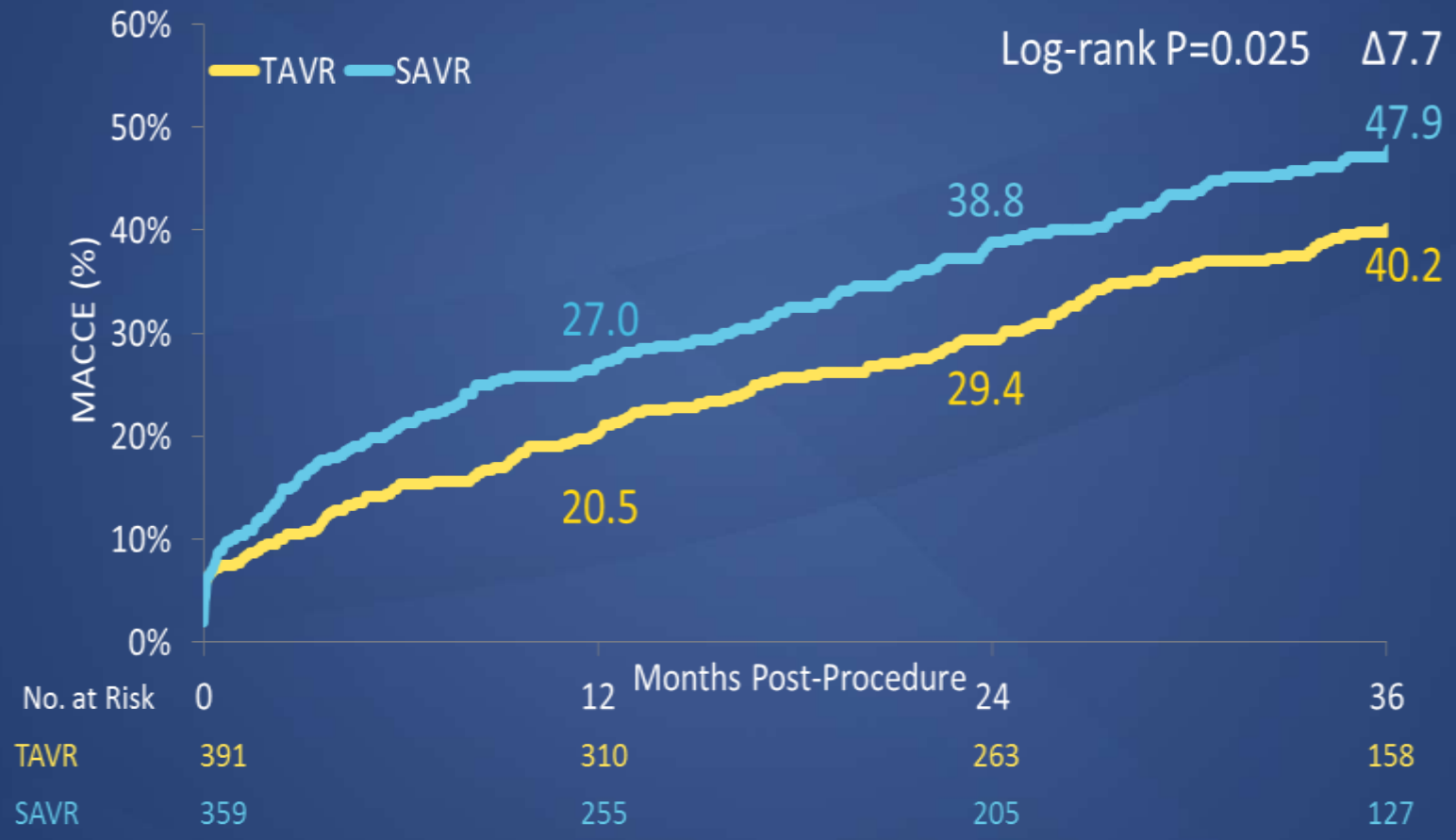
All-Cause Mortality – STS ≤ 7%



Deeb GM et al. J Am Coll Cardiol. 2016;67(22):2565-74.

CoreValve US Pivotal Trial– 3 year result

MACCE



Deeb GM et al. J Am Coll Cardiol. 2016;67(22):2565-74.

CoreValve US Pivotal Trial– 3 year result

Valve Hemodynamics *(site-reported)*

TAVR had significantly better valve performance vs SAVR at all follow-ups (P<0.001)

Deeb GM et al. J Am Coll Cardiol. 2016;67(22):2565-74.

CoreValve US Pivotal Trial– 3 year result

Hemodynamic Signals *(site-reported)*

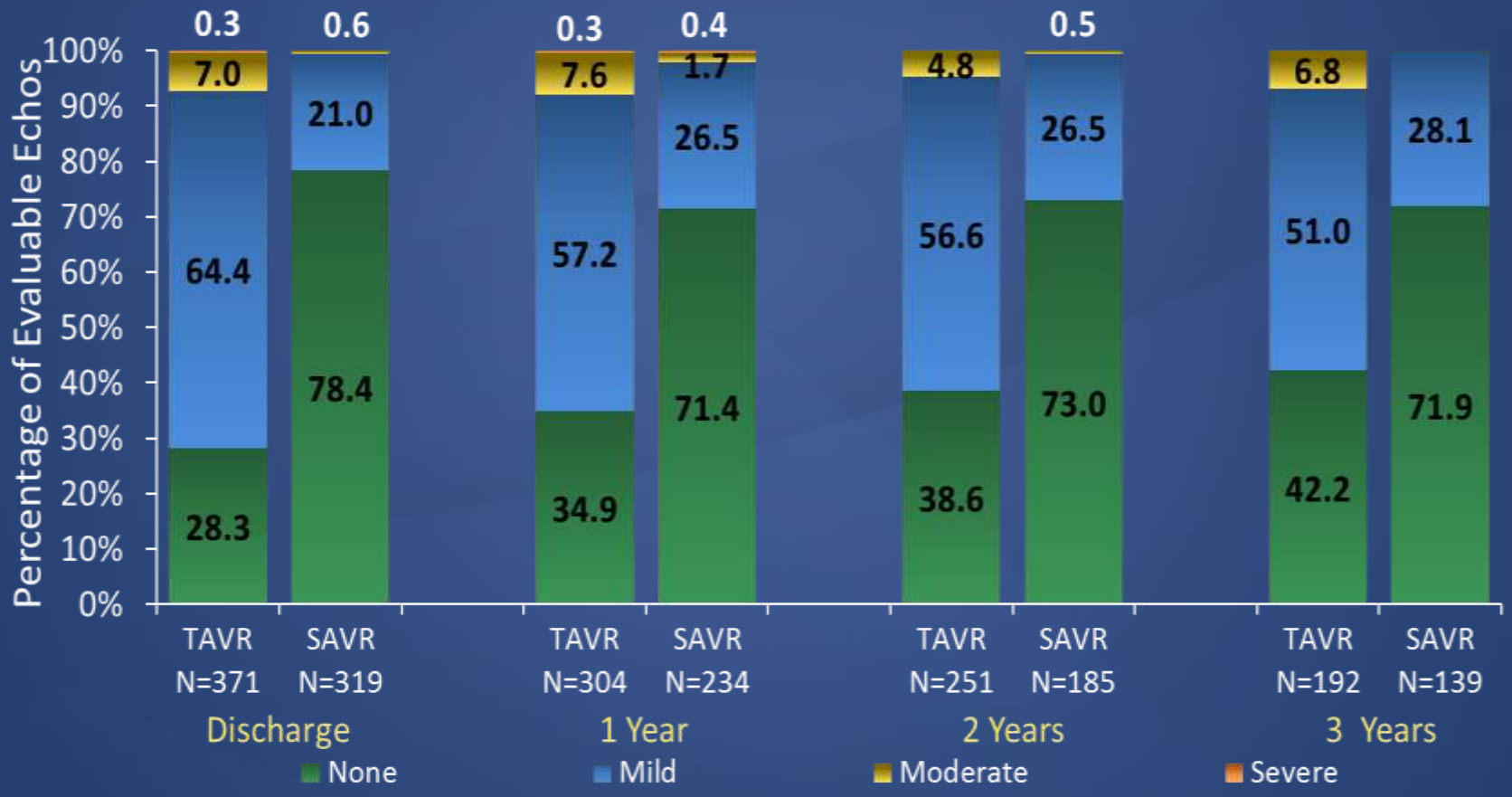
Mean AV Gradients for Patients With >50% Increase From 1 Month to 3 Years

Deeb GM et al. J Am Coll Cardiol. 2016;67(22):2565-74.

CoreValve US Pivotal Trial– 3 year result

Total Aortic Regurgitation *(site reported)*

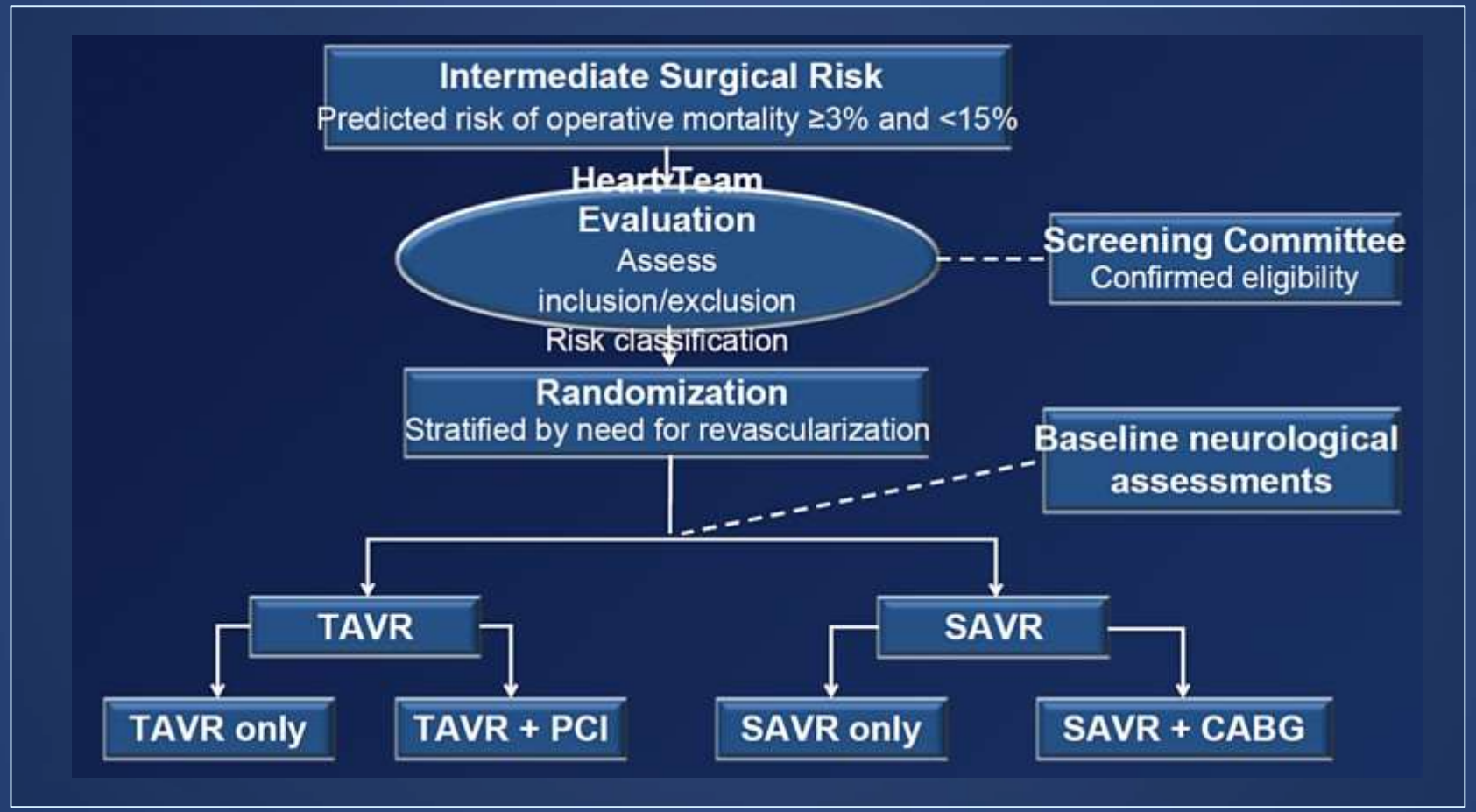
Significantly less AR with SAVR vs. TAVR at Each Time Point (P<0.001)



Deeb GM et al. J Am Coll Cardiol. 2016;67(22):2565-74.

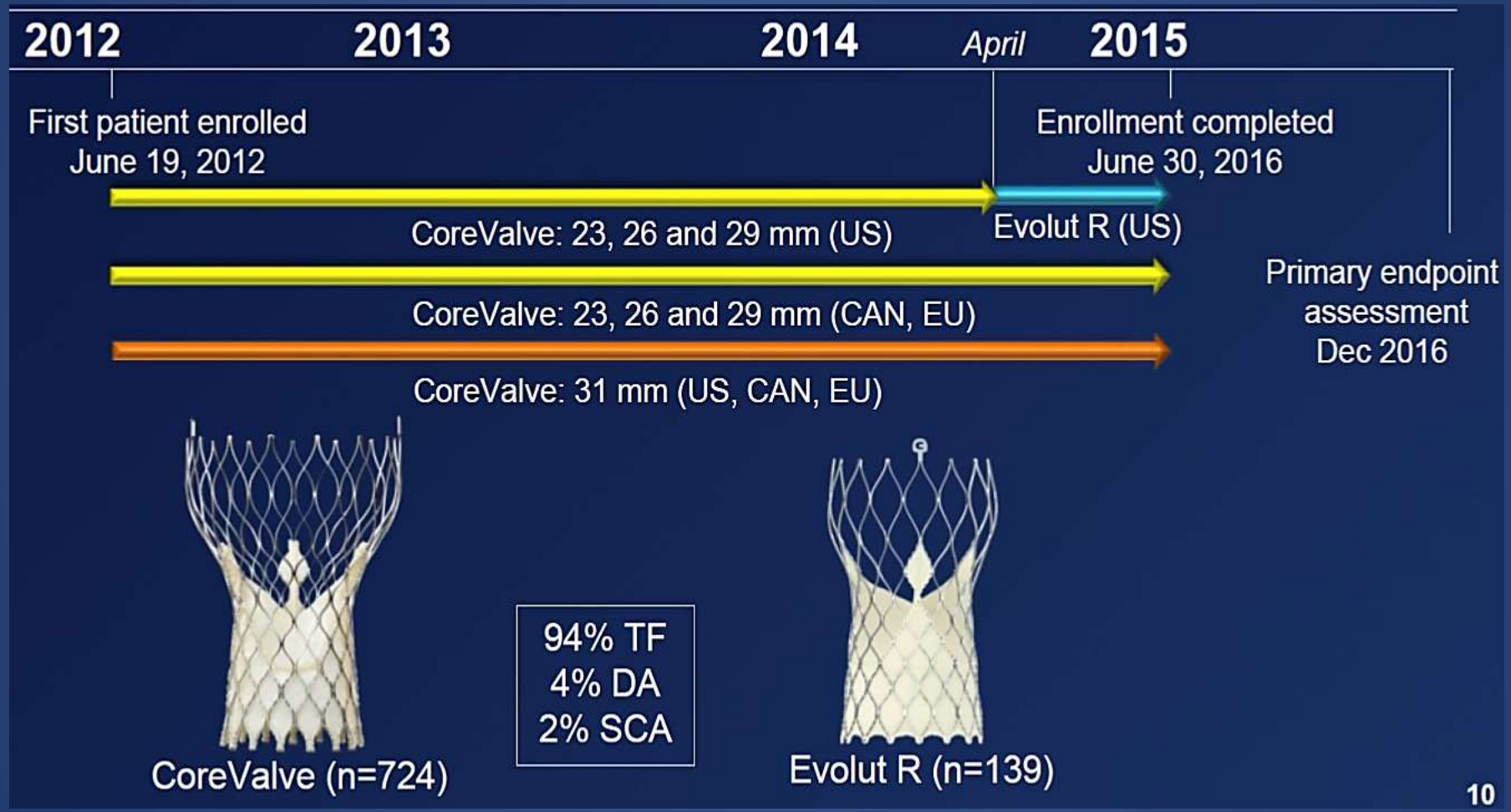
SURTAVI TRIAL

Trial Design



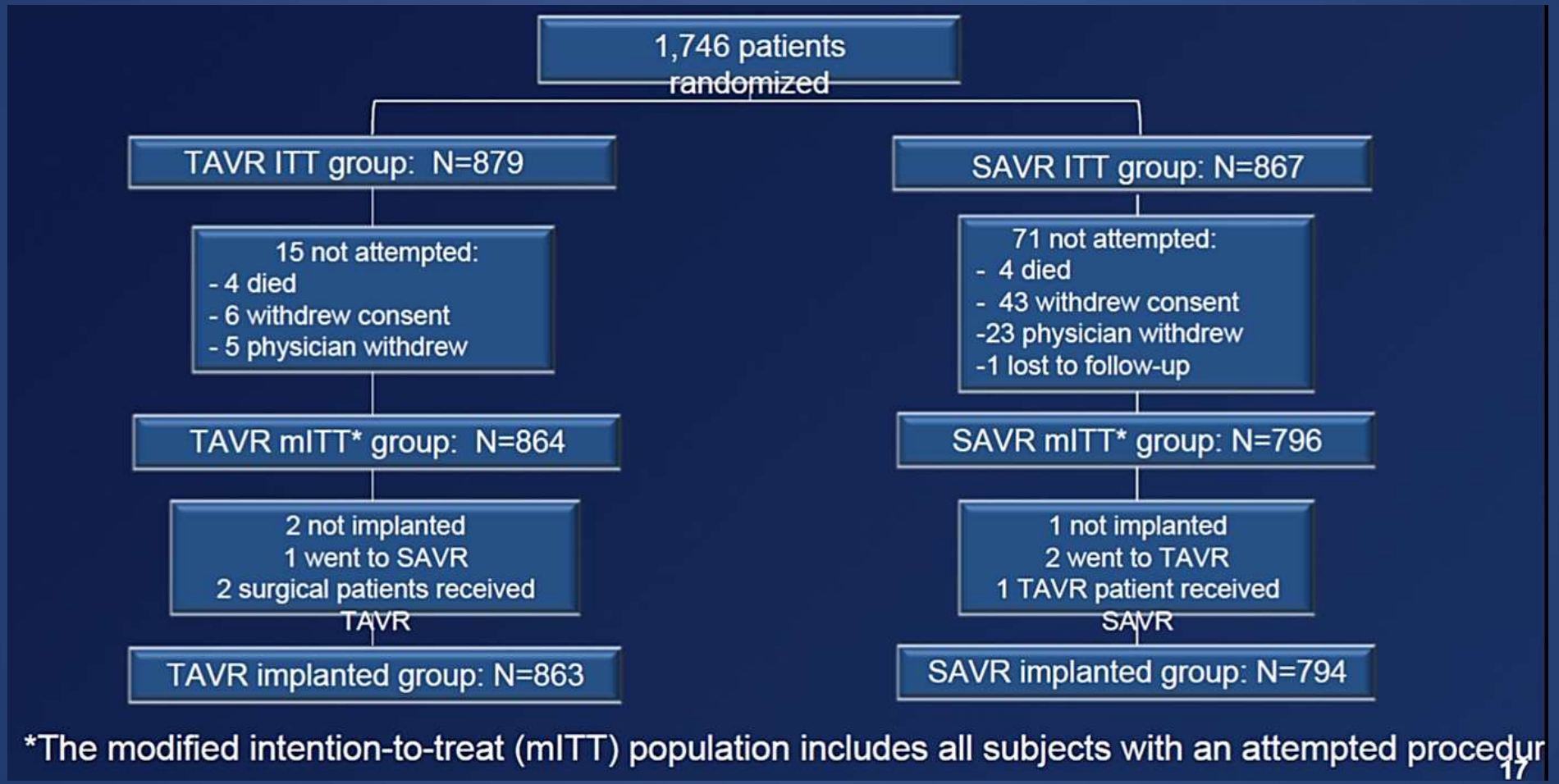
MJ Reardon et al. N Eng J Med. March 17, 2017

Study Timeline



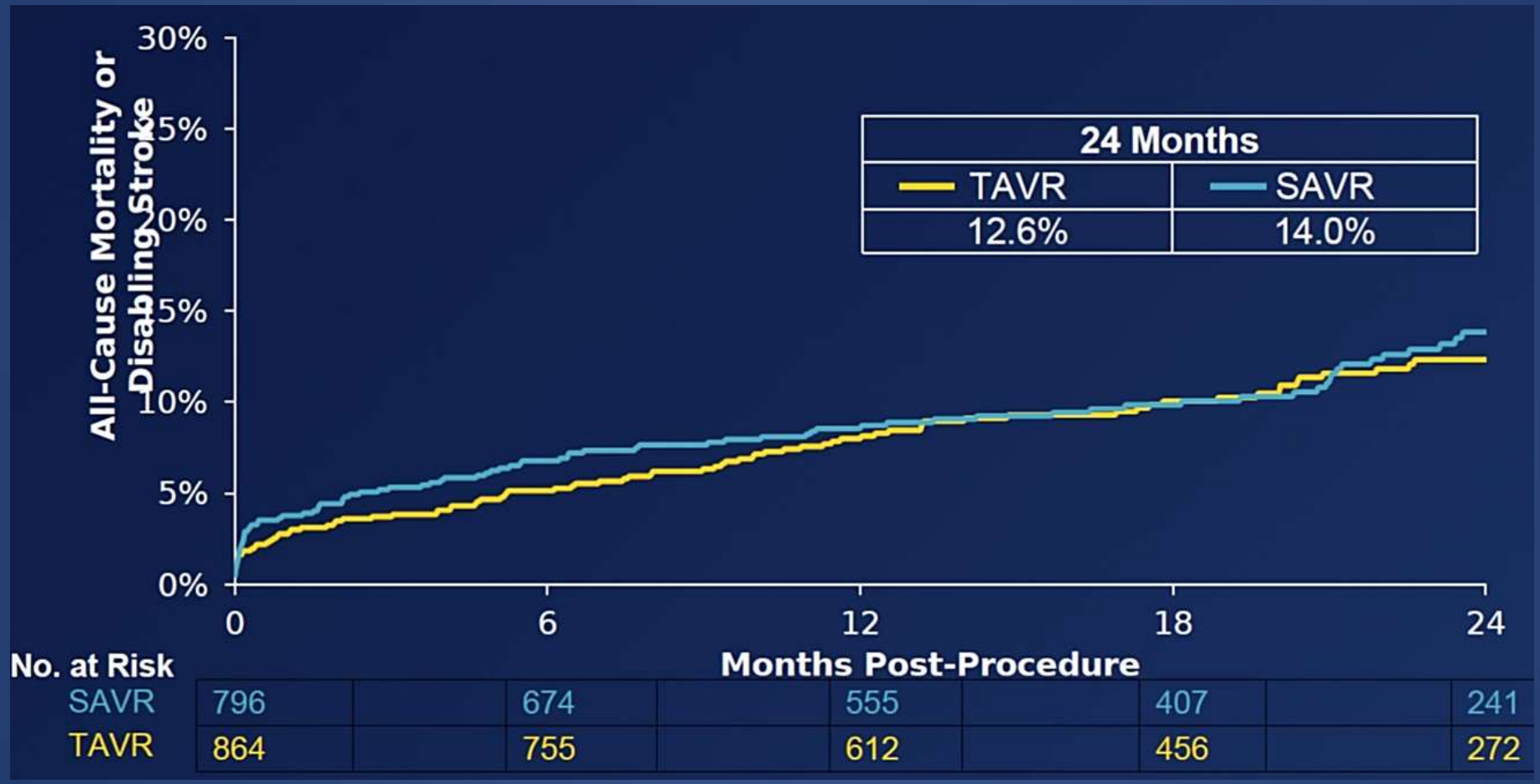
MJ Reardon et al. N Eng J Med. March 17, 2017

Patient Flow



MJ Reardon et al. N Eng J Med. March 17, 2017

All-Cause Mortality or Disabling Stroke



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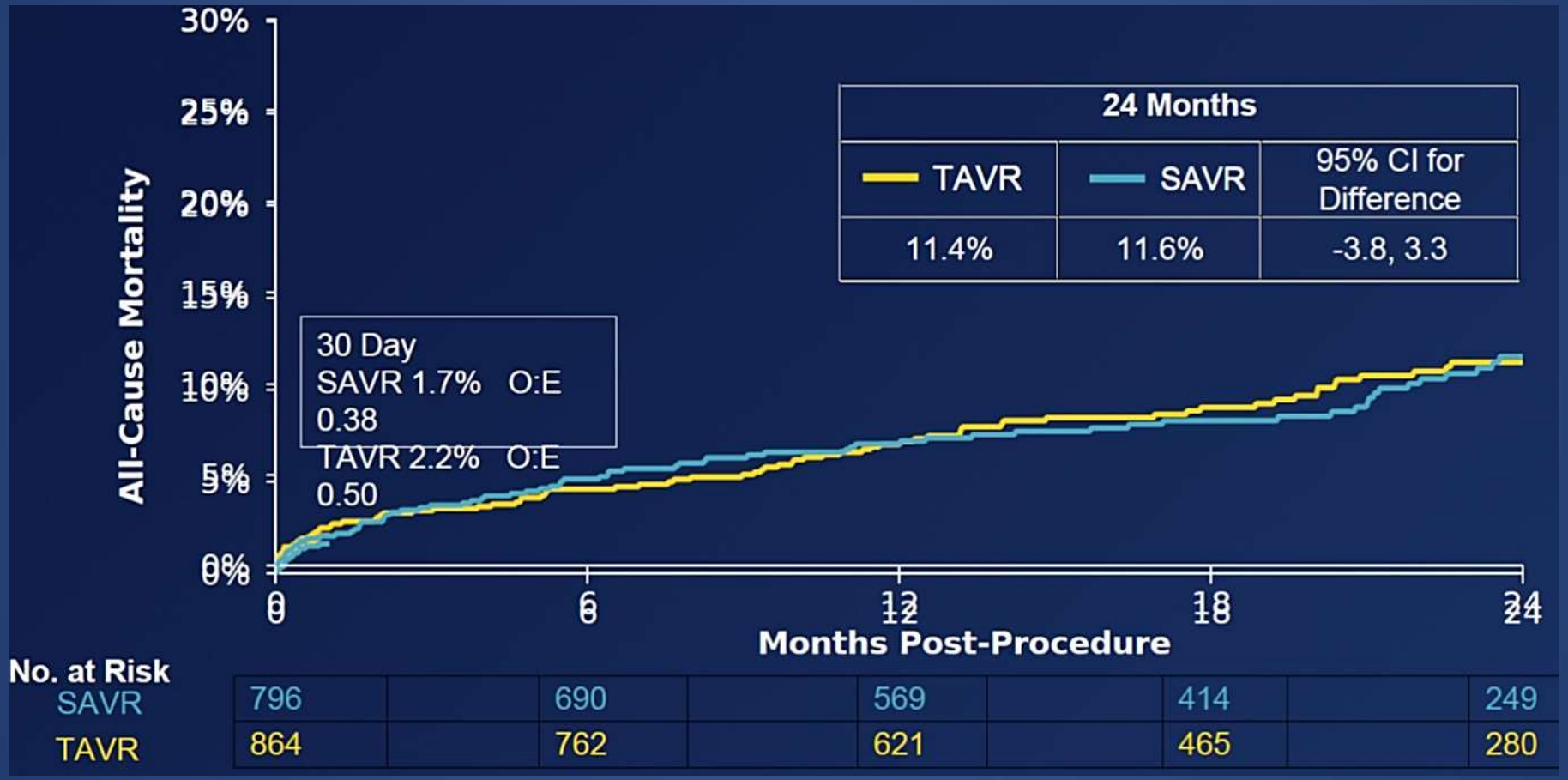
All-Cause Mortality



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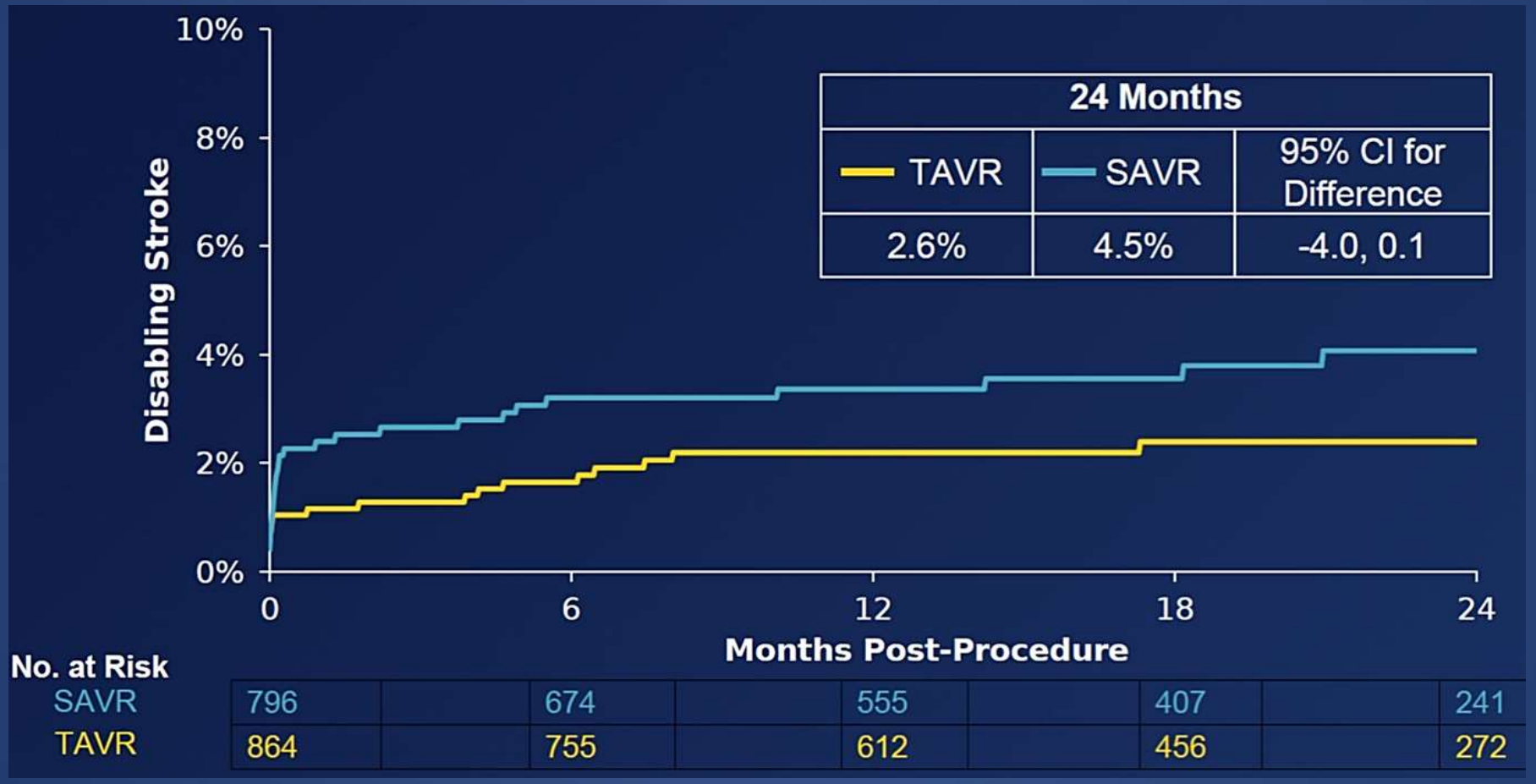
Disabling Stroke



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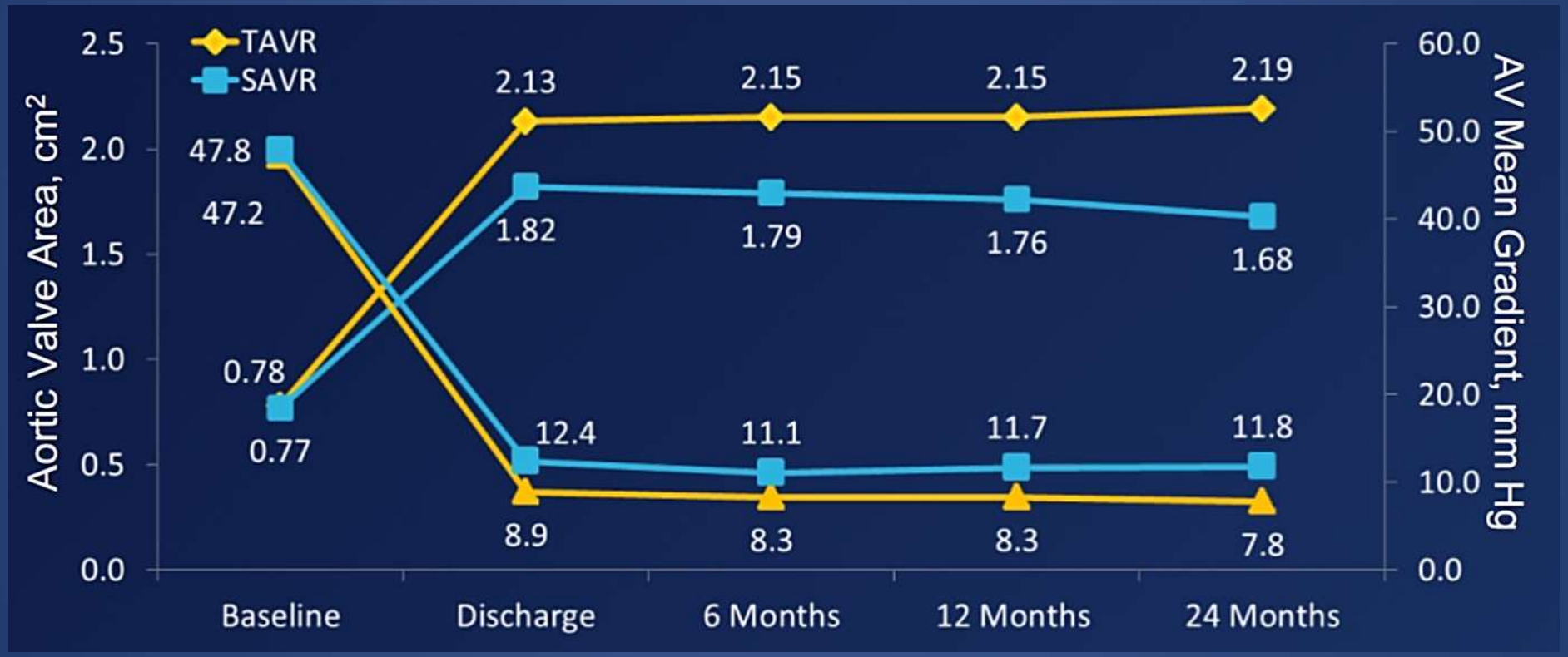
Hemodynamics

TAVR had significantly better valve performance vs SAVR at all follow-ups



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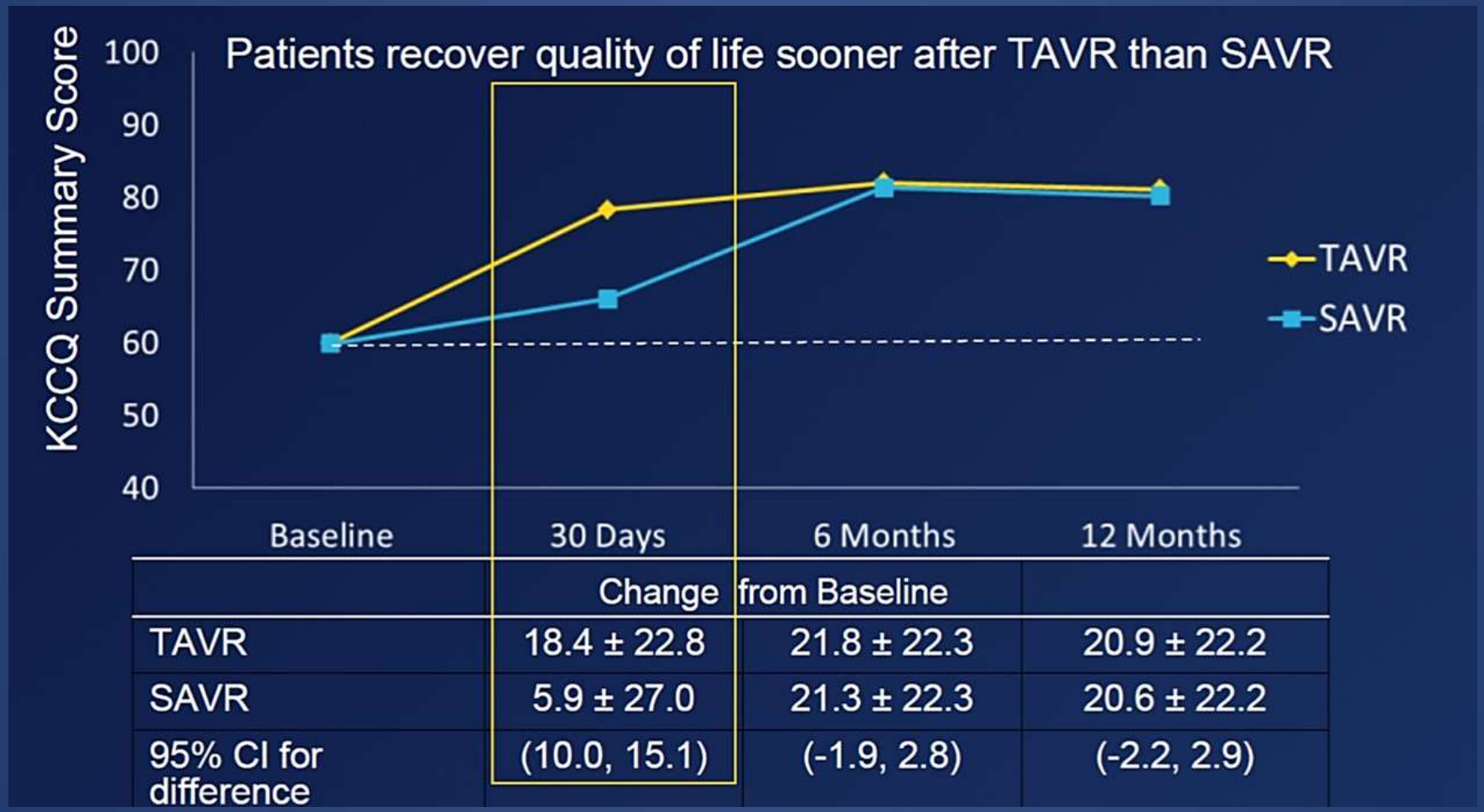
KCCQ Summary Score Over Time



	Change from Baseline		
TAVR	18.4 ± 22.8	21.8 ± 22.3	20.9 ± 22.2
SAVR	5.9 ± 27.0	21.3 ± 22.3	20.6 ± 22.2
95% CI for difference	(10.0, 15.1)	(-1.9, 2.8)	(-2.2, 2.9)

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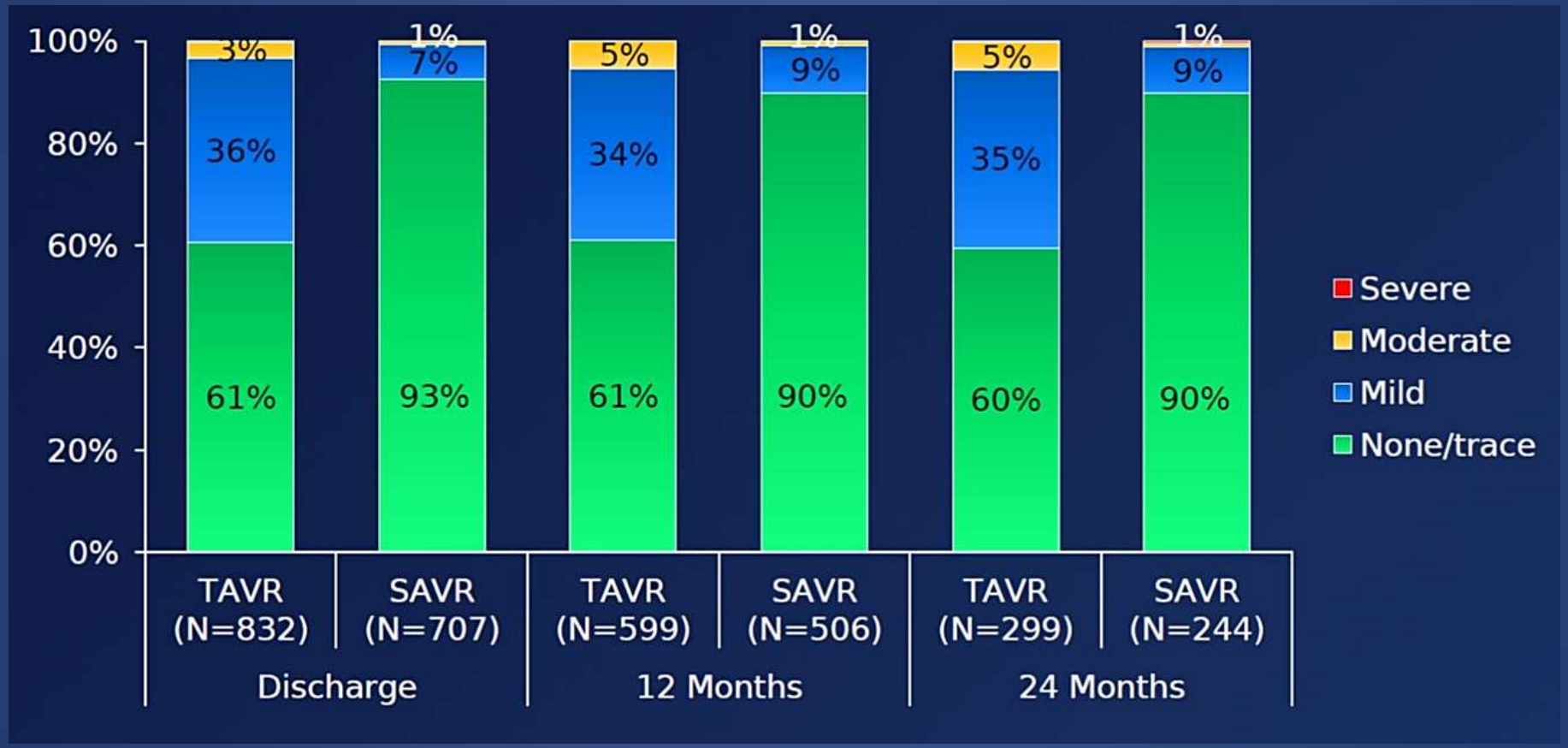
Total Aortic Regurgitation



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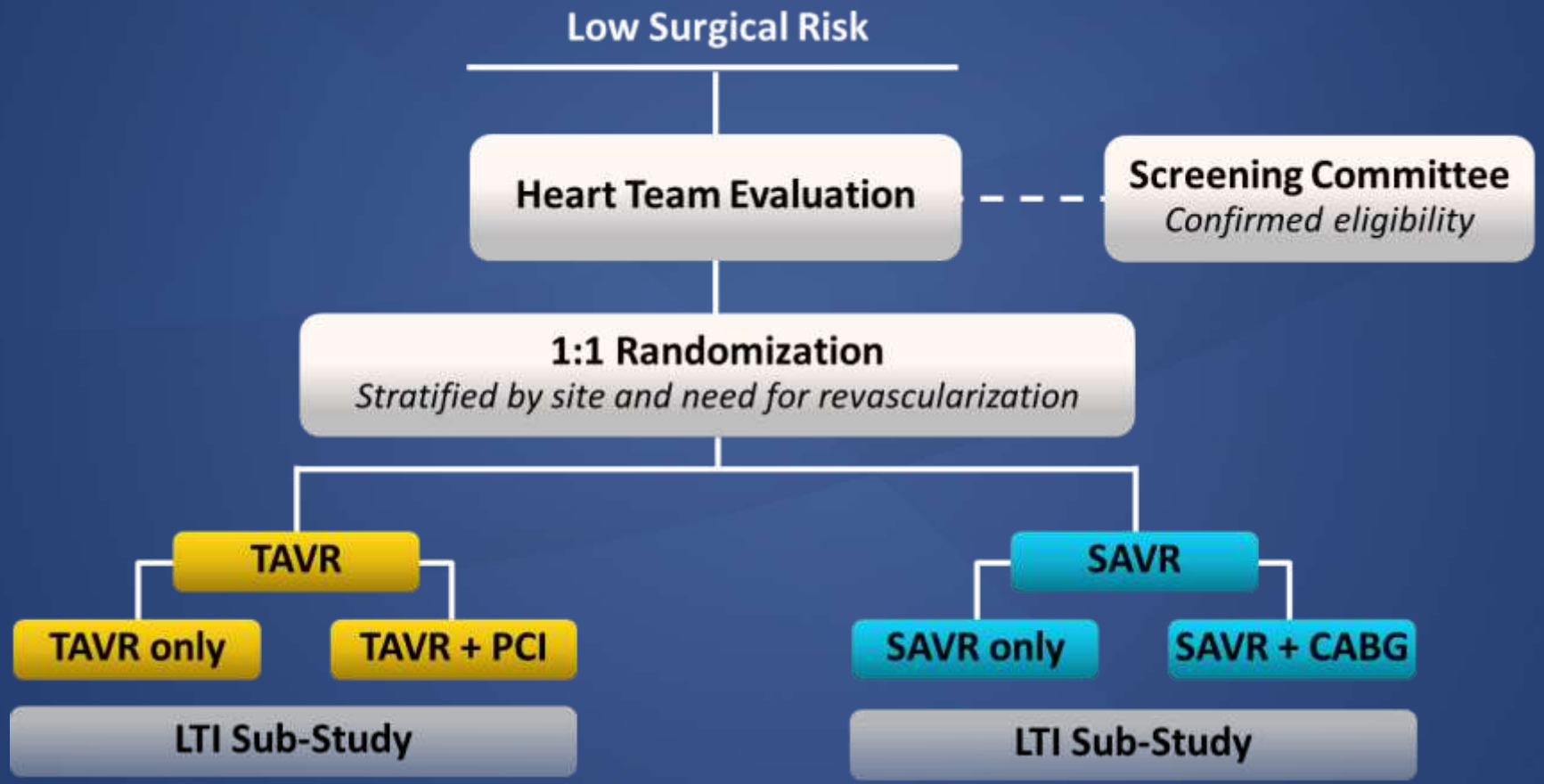
Evolut™ Low Risk Trial

Evolut Low Risk Trial

Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients

Evolut™ Low Risk Trial

Study Design



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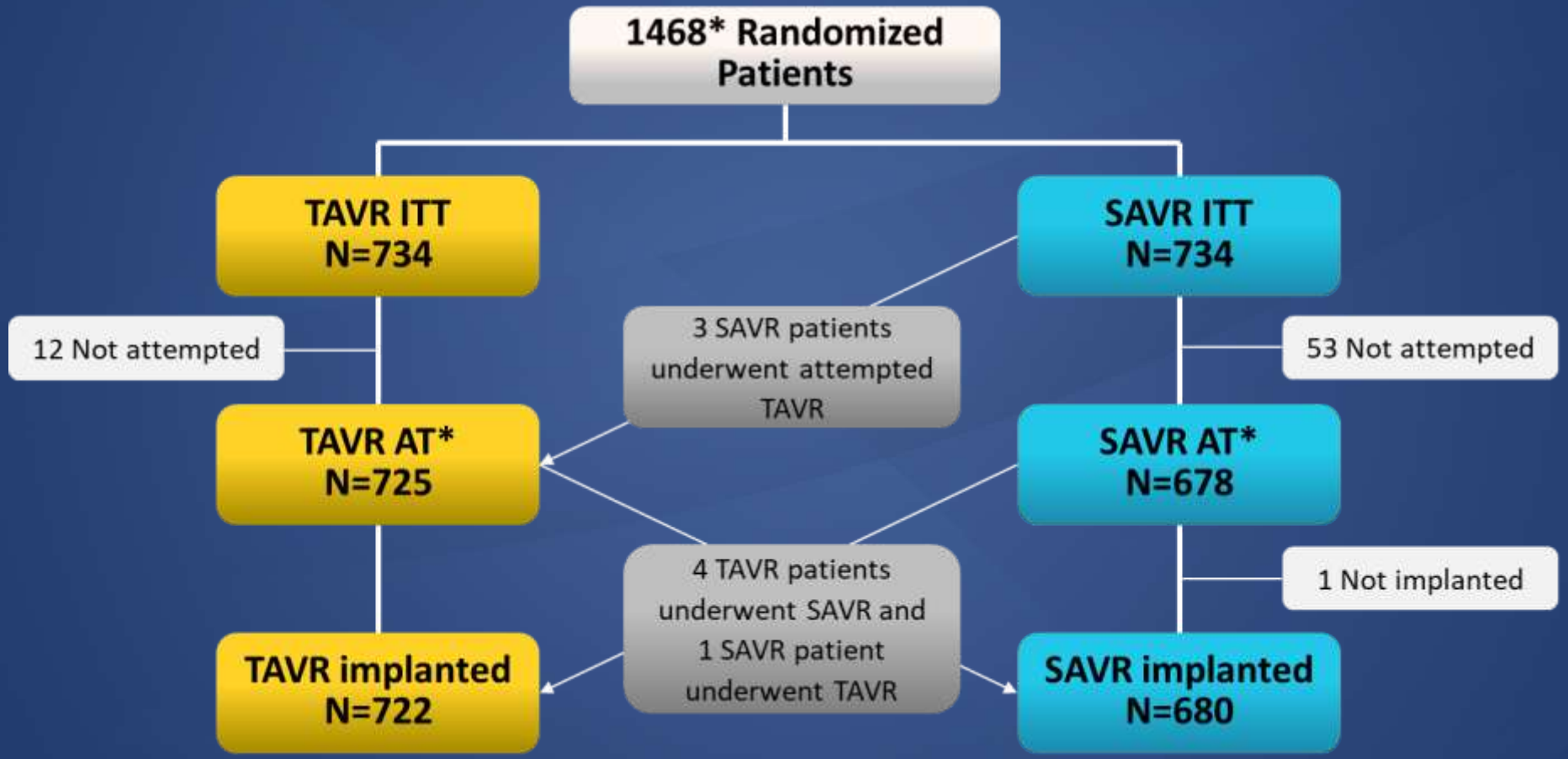
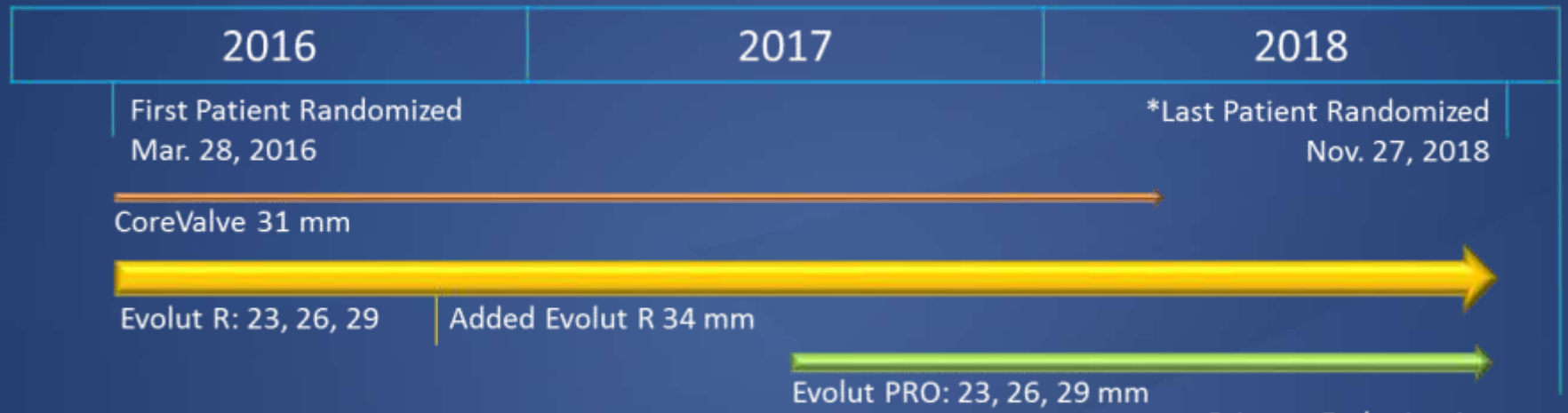
Patient Flow



*Additional patients were randomized to permit completion of the LTI substudy and to enroll a Japanese cohort.

Study Timeline and Valves Studied



CoreValve 31 = 3.6%	Evolut R = 74.1%	Evolut PRO = 22.3%

Vascular access
- 99% transfemoral
- 0.6% subclavian
- 0.4% direct aortic

*For this analysis

Evolut™ Low Risk Trial

Evolut Low Risk Trial
Baseline Characteristics

Mean ± SD or %	TAVR (N=725)	SAVR (N=678)
Age, years	74.1 ± 5.8	73.6 ± 5.9
Female sex	36.0	33.8
Body surface area, m^2	2.0 ± 0.2	2.0 ± 0.2
STS PROM, %	1.9 ± 0.7	1.9 ± 0.7
NYHA Class III or IV	25.1	28.5
Hypertension	84.8	82.6
Chronic lung disease (COPD)	15.0	18.0
Cerebrovascular disease	10.2	11.8
Peripheral arterial disease	7.5	8.3

There are no significant differences between groups.

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Baseline Cardiac Rissk Factors

Mean ± SD or %	TAVR (N=725)	SAVR (N=678)
SYNTAX Score	1.9 ± 3.7	2.1 ± 3.9
Permanent pacemaker, CRT or ICD	3.2	3.8
Prior CABG	2.5	2.1
Previous PCI	14.2	12.8
Previous myocardial infarction	6.6	4.9
Atrial fibrillation/flutter	15.4	14.5
Aortic valve gradient, mm Hg	47.0 ± 12.1	46.6 ± 12.2
Aortic Valve area, cm^2	0.8 ± 0.2	0.8 ± 0.2
Left ventricular ejection fraction, %	61.7 ± 7.9	61.9 ± 7.7

There are no significant differences between groups.

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TAVR Procedural Data

%	TAVR (N=724)
General anesthesia	56.9
Iliofemoral access	99.0
Embolic protection device used	1.2
Pre-TAVR balloon dilation	34.9
Post-TAVR balloon dilation	31.3
More than 1 valve used	1.2
Partial or complete repositioning of the valve (Evolut/PRO only)	37.3
Staged or concomitant PCI performed	6.9

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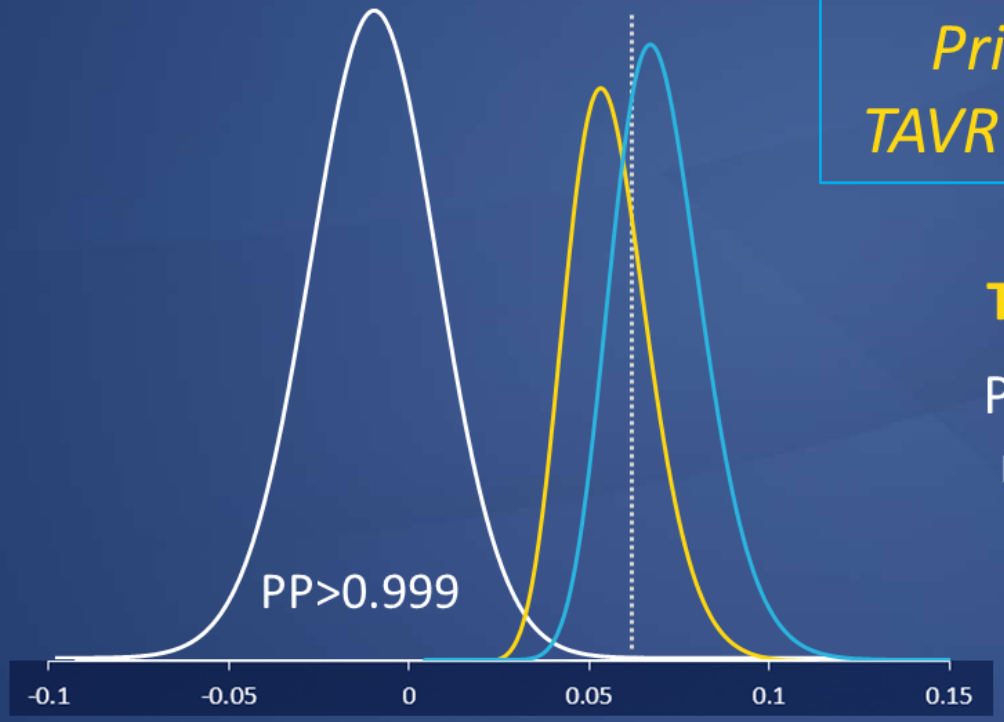
Primary Endpoint

All-Cause Mortality or Disabling Stroke at 2 Years



Primary Endpoint Met
TAVR is noninferior to SAVR

TAVR 5.3% **SAVR 6.7%**

Posterior probability of noninferiority > 0.999

TAVR –SAVR difference = -1.4% (95% BCI; -4.9, 2.1)

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Hierarchical Secondary Endpoints

All Noninferiority and Superiority Endpoints Met

	TAVR	SAVR	Difference TAVR–SAVR	Posterior Probability
Noninferiority (margin)			(90% BCI)	
Mean gradient at 12 months (5 mmHg)	8.6 ± 3.7	11.2 ± 4.9	-2.6 (-3.1, -2.1)	> 0.999 ✓
Mean EOA at 12 months (0.1 cm^2)	2.3 ± 0.7	2.0 ± 0.6	0.3 (0.2, 0.4)	> 0.999 ✓
Mean NYHA class change (12 months –Baseline) (0.375)	0.9 ± 0.7	1.0 ± 0.7	-0.1 (-0.2, 0.0)	> 0.999 ✓
Mean KCCQ change (12 months –Baseline) (5)	22.2 ± 20.3	20.9 ± 21.0	1.3 (-1.2, 3.8)	> 0.999 ✓
Superiority			(95% BCI)	
Mean gradient at 12 months, mmHg	8.6 ± 3.7	11.2 ± 4.9	-2.6 (-3.2, -2.0)	> 0.999 ✓
Mean EOA at 12 months, cm^2	2.3 ± 0.7	2.0 ± 0.6	0.3 (0.2, 0.4)	> 0.999 ✓
Mean KCCQ change (30 Days–Baseline)	20.0 ± 21.1	9.1 ± 22.3	10.9 (8.6, 13.2)	> 0.999 ✓

Evolut™ Low Risk Trial

Evolut Low Risk Trial

Clinical Outcomes at 30 Days

Bayesian rates as %	TAVR (N=725)	SAVR (N=678)	(95% BCI for Difference)
30-Day composite safety endpoint*	5.3	10.7	(-8.3, -2.6)
All-cause mortality	0.5	1.3	(-1.9, 0.2)
Disabling stroke*	0.5	1.7	(-2.4, -0.2)
Life-threatening or disabling bleeding*	2.4	7.5	(-7.5, -2.9)
Acute kidney injury, stage 2-3*	0.9	2.8	(-3.4, -0.5)
Major vascular complication	3.8	3.2	(-1.4, 2.5)
Atrial fibrillation*	7.7	35.4	(-31.8, -23.6)
Permanent pacemaker implant*	17.4	6.1	(8.0, 14.7)
All-cause mortality or disabling stroke*	0.8	2.6	(-3.2, -0.5)
All stroke	3.4	3.4	(-1.9, 1.9)
Aortic valve reintervention	0.4	0.4	(-0.8, 0.7)

* Significantly favors TAVR; * Significantly favors SAVR

BCI = Bayesian credible interval

Evolut™ Low Risk Trial

Evolut Low Risk Trial

Clinical Outcomes at 1 Year

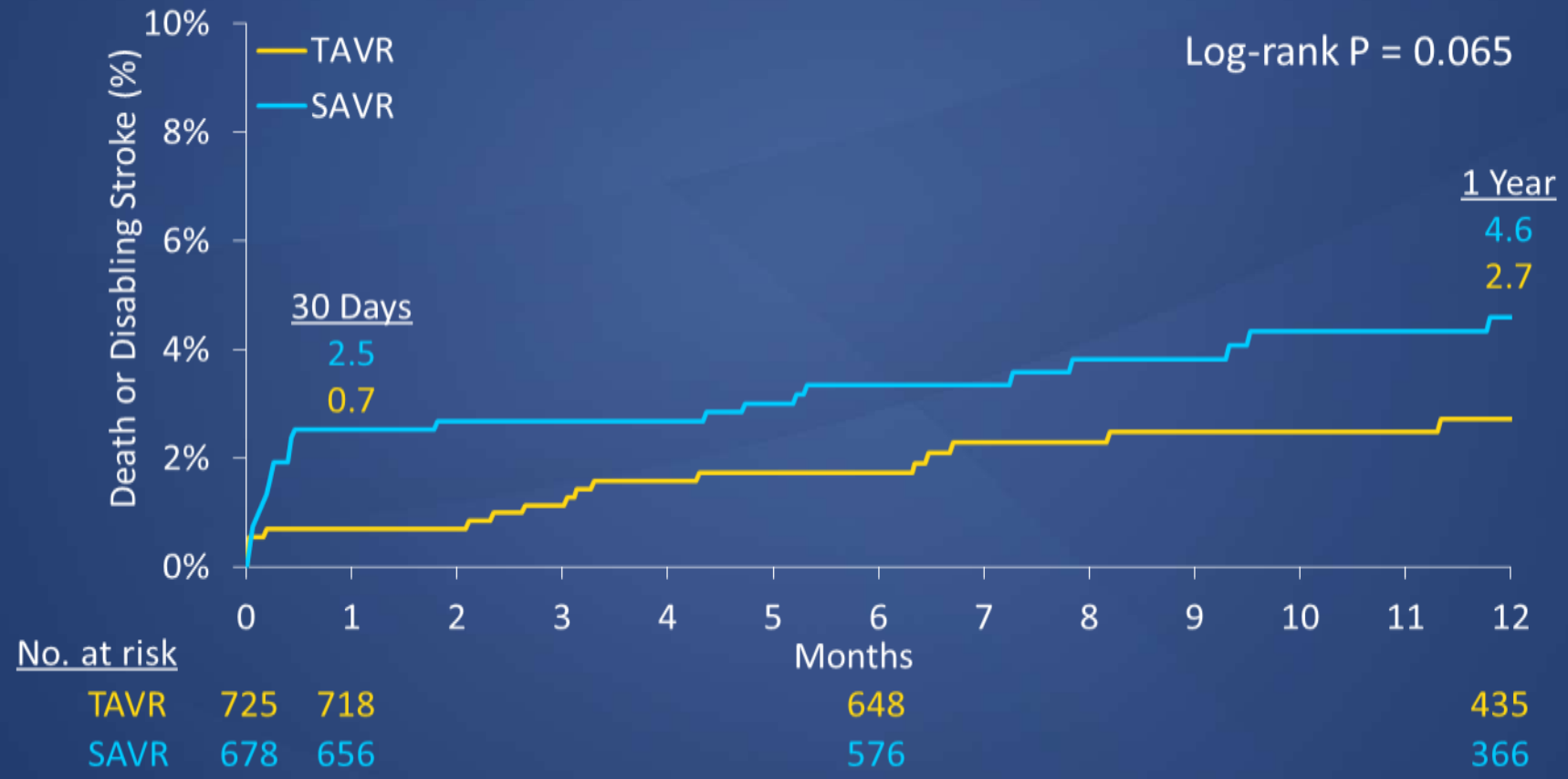
Bayesian rates as %	TAVR (N=725)	SAVR (N=678)	(95% BCI for Difference)
All-cause mortality or disabling stroke	2.9	4.6	(-4.0, 0.4)
All-cause mortality	2.4	3.0	(-2.6, 1.3)
Cardiovascular mortality	1.7	2.6	(-2.7, 0.7)
All stroke	4.1	4.3	(-2.4, 1.9)
Disabling stroke*	0.8	2.4	(-3.1, -0.3)
Transient ischemia attack	1.7	1.8	(-1.6, 1.3)
Myocardial infarction	1.7	1.6	(-1.3, 1.5)
Endocarditis	0.2	0.4	(-0.9, 0.5)
Valve thrombosis	0.2	0.3	(-0.9, 0.5)
Aortic valve reintervention	0.7	0.6	(-1.0, 0.9)
Heart failure hospitalization*	3.2	6.5	(-5.9, -1.0)

* Significantly favors TAVR

BCI = Bayesian credible interval

Evolut Low Risk Trial

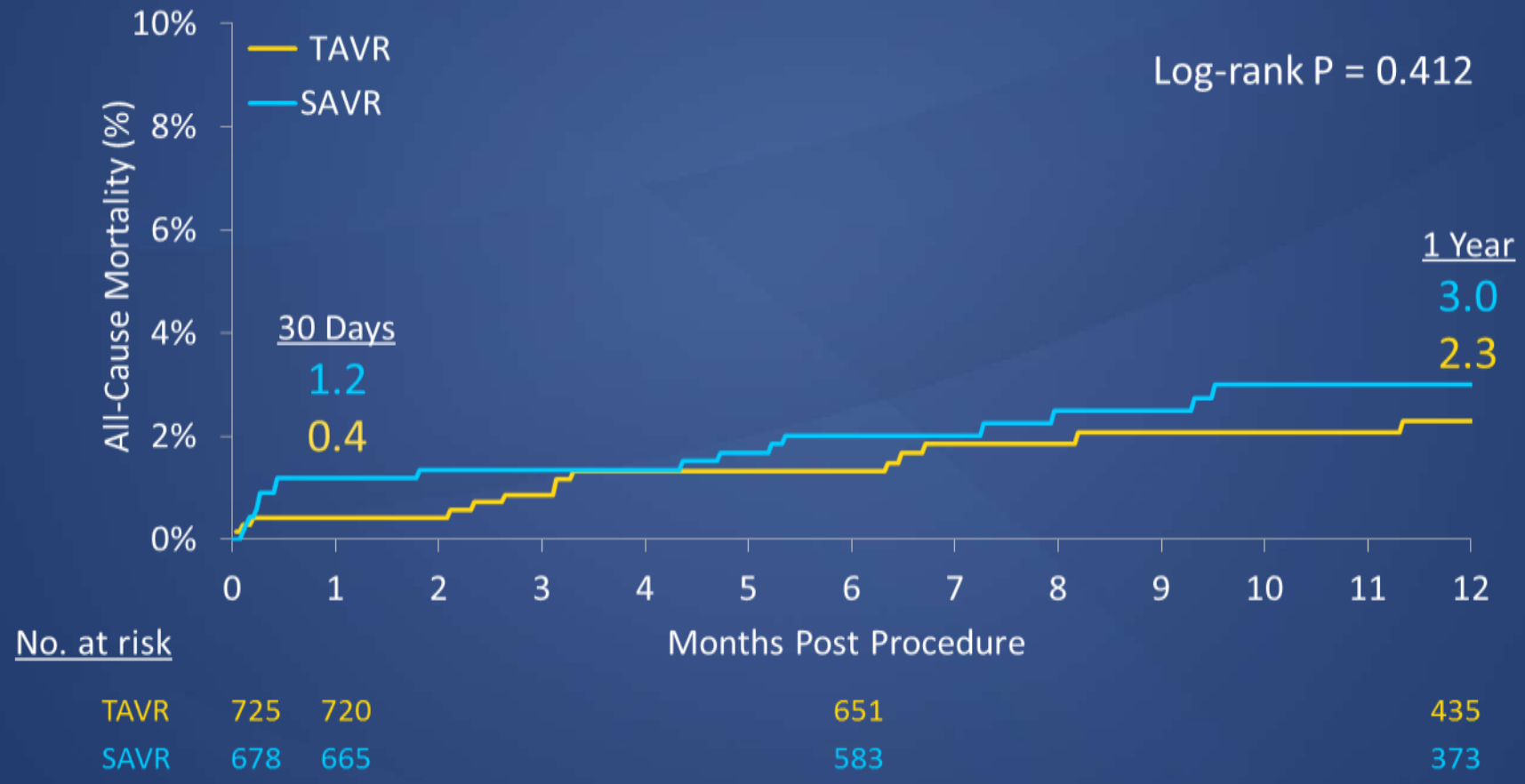
K-M All-Cause Mortality or Disabling Stroke at 1 Year



Evolut™ Low Risk Trial

Evolut Low Risk Trial

K-M Rates of All-Cause Mortality at 1 Year



No. at risk

TAVR	725	720	651	435
SAVR	678	665	583	373

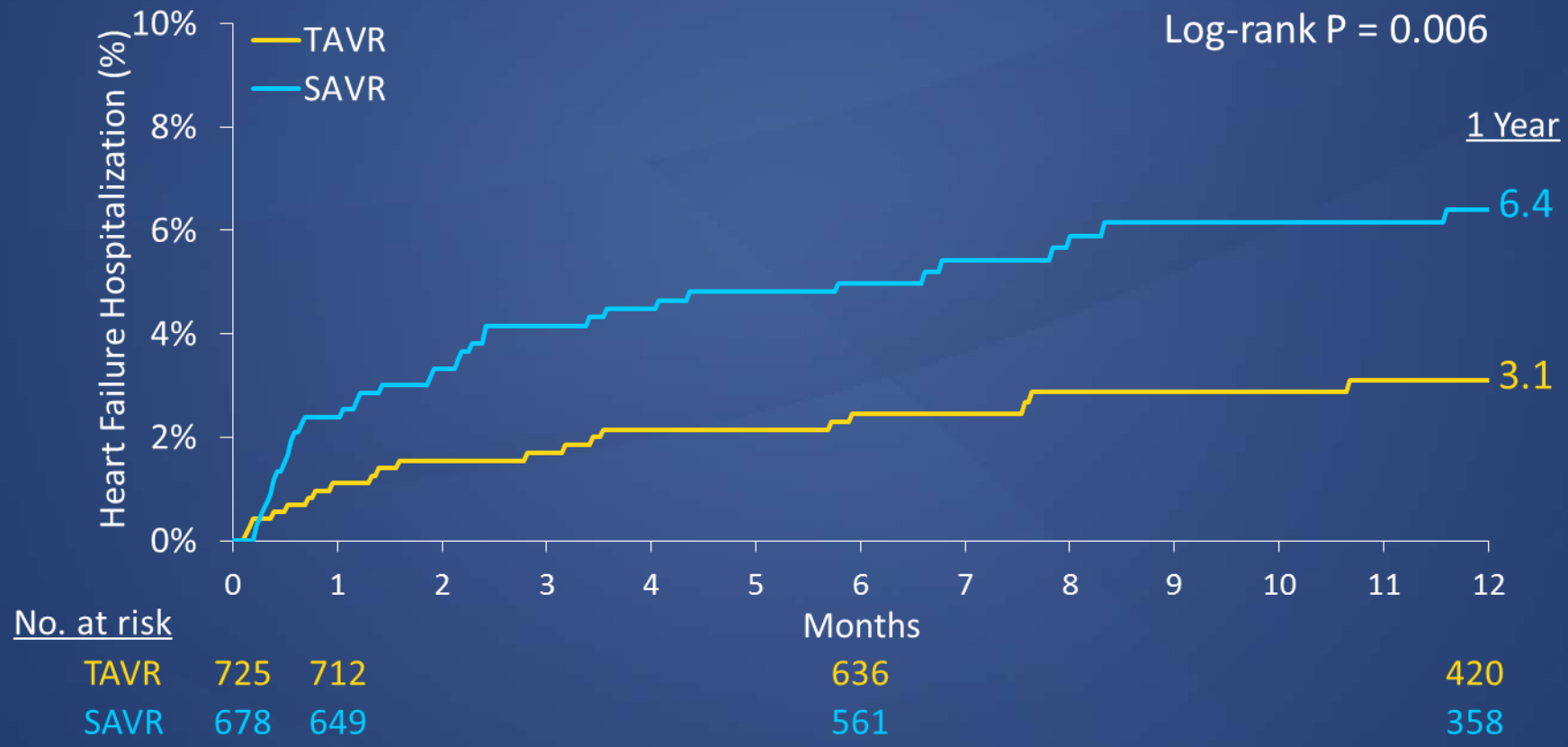
Evolut Low Risk Trial

K-M Disabling Stroke at 1 Year

Evolut™ Low Risk Trial

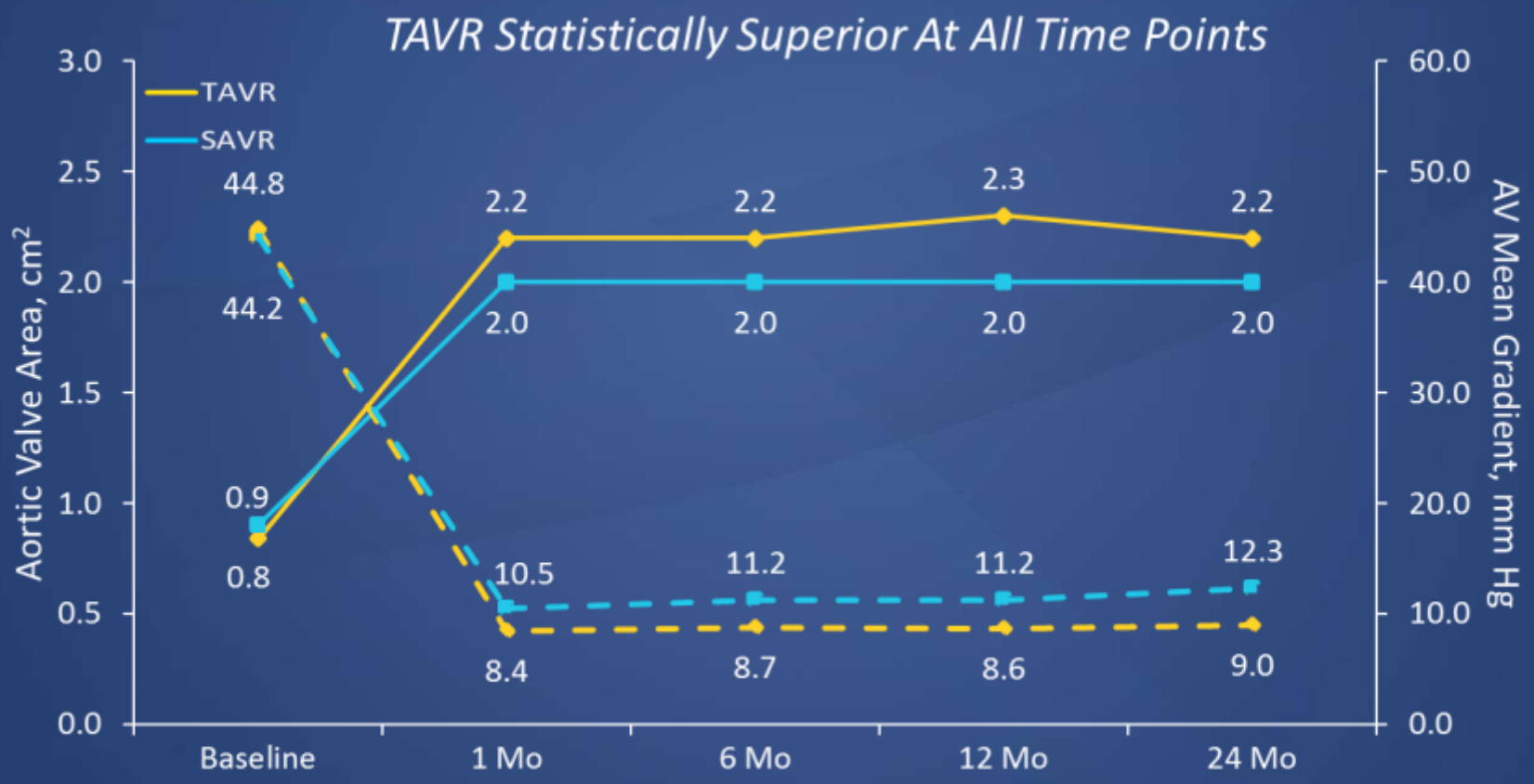
Evolut Low Risk Trial

K-M Heart Failure Hospitalization at 1 Year



Evolut™ Low Risk Trial

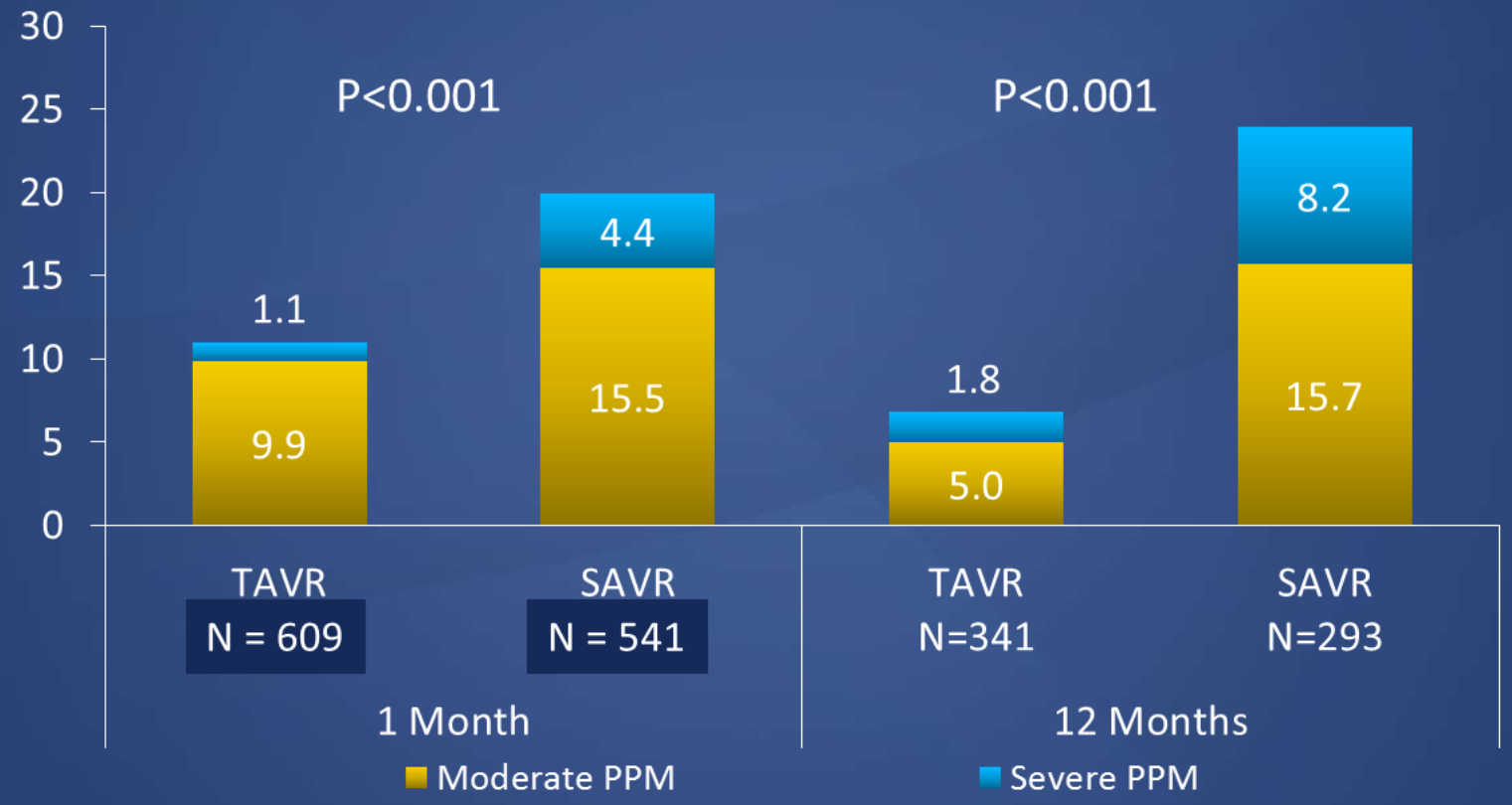
Valve Hemodynamics



Implanted population. Core lab assessments.

Evolut™ Low Risk Trial

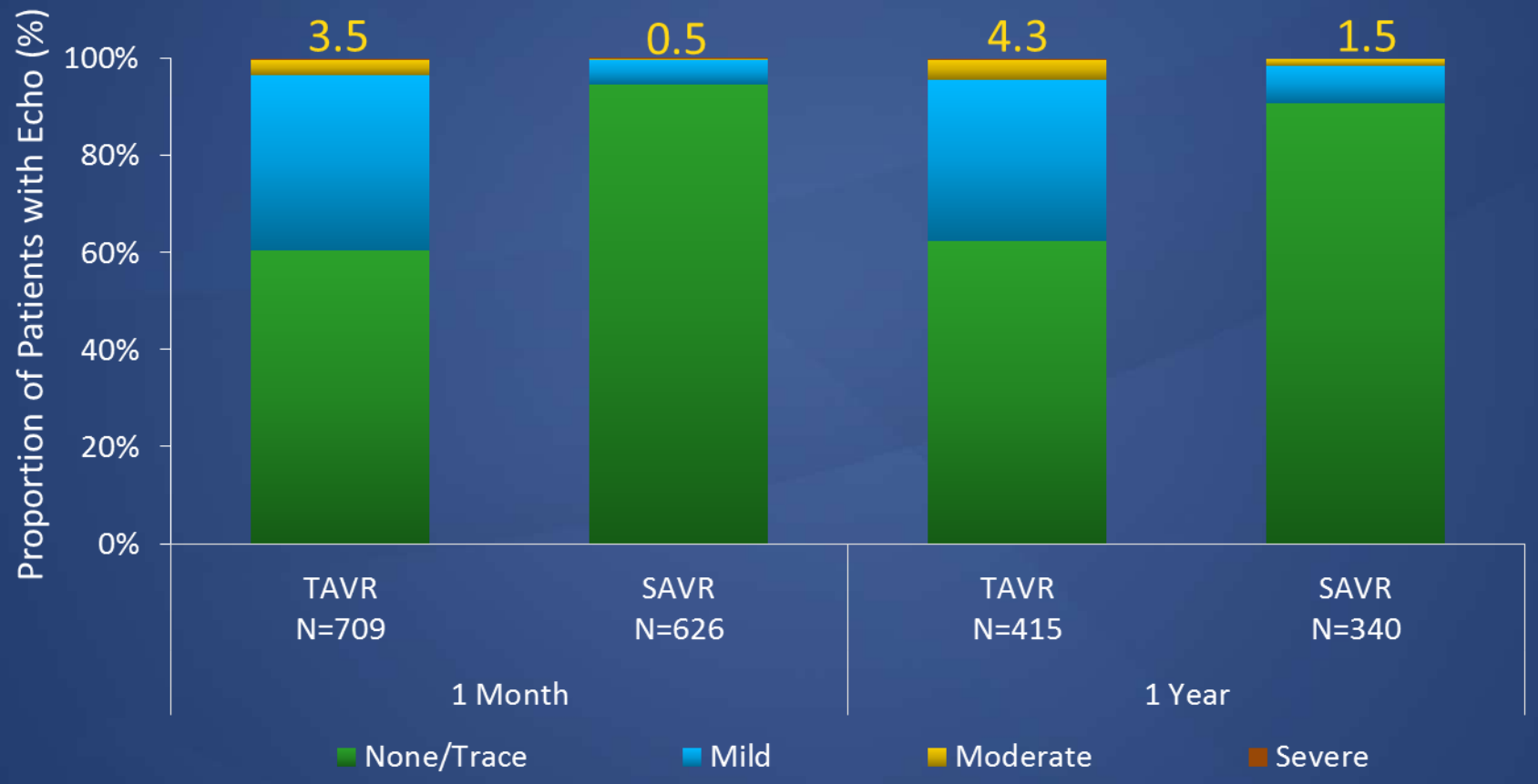
Prosthesis-Patient Mismatch



Implant population. Core lab assessments.

Total Aortic Valve Regurgitation

Evolut™ Low Risk Trial



Implant population. Core lab assessments.

Evolut™ Low Risk Trial

KCCQ Summary Score

Patients Recover Quality of Life Sooner After TAVR

	Change from Baseline		
TAVR	20.0 ± 21.1	21.9 ± 21.2	22.2 ± 20.3
SAVR	9.1 ± 22.3	20.5 ± 20.5	20.9 ± 20.9
95% BCI for difference	(8.6, 13.2)	(-1.0, 3.8)	(-1.6, 4.3)

Evolut R
self-expandable THV

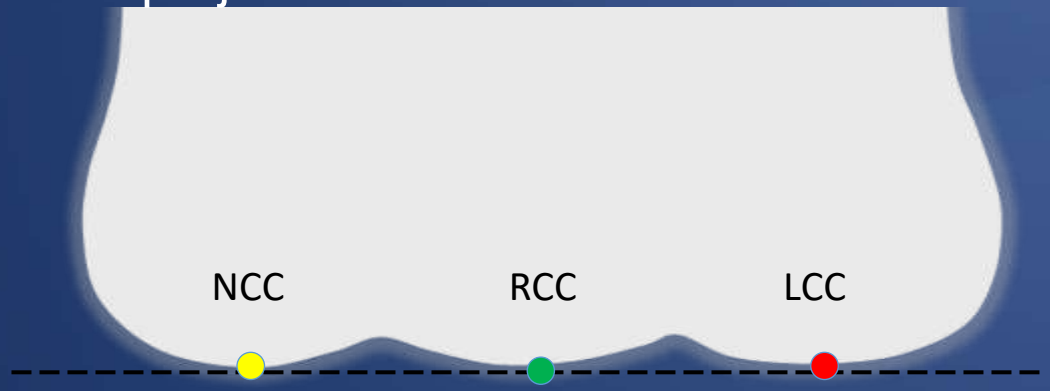
Pre-Procedure CT Planning

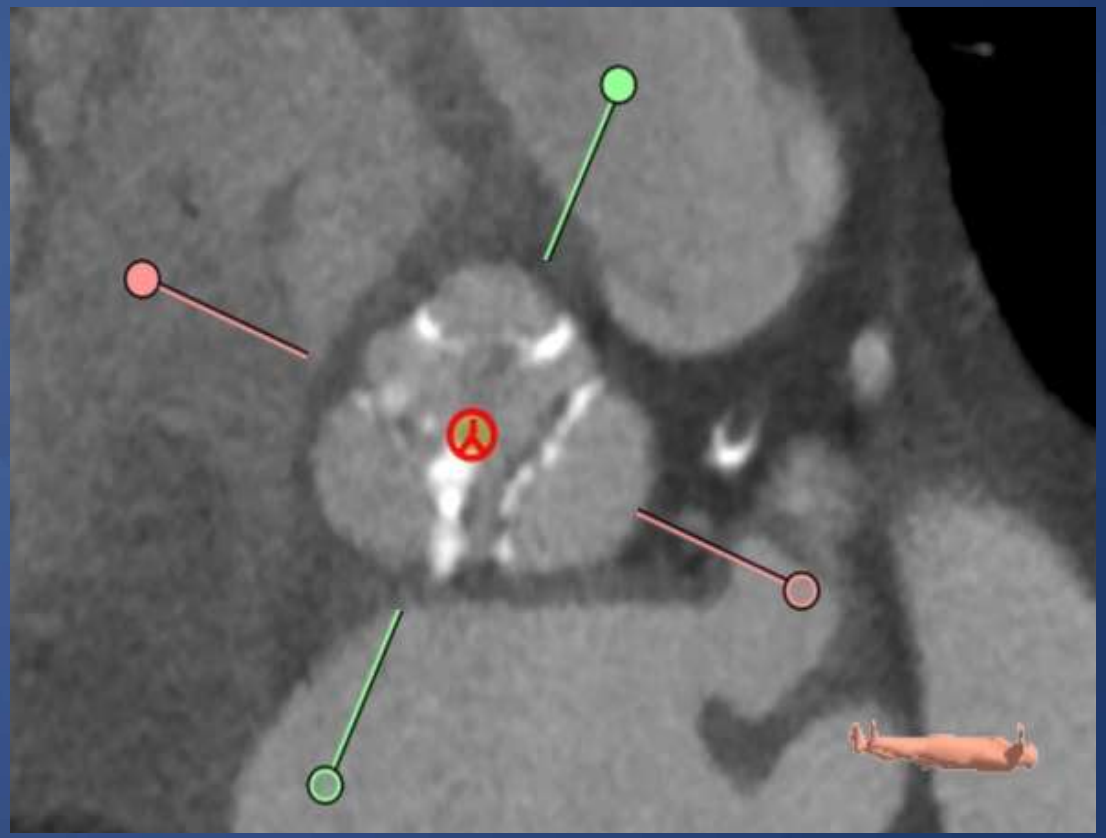
BASAL ANNULAR PLANE

The cusp overlap technique requires high quality gated CT with contrast; free from movement artifacts and slice misregistration.

Set basal annular plane by placing markers at lowest point in the center of each cusp in short axis view.

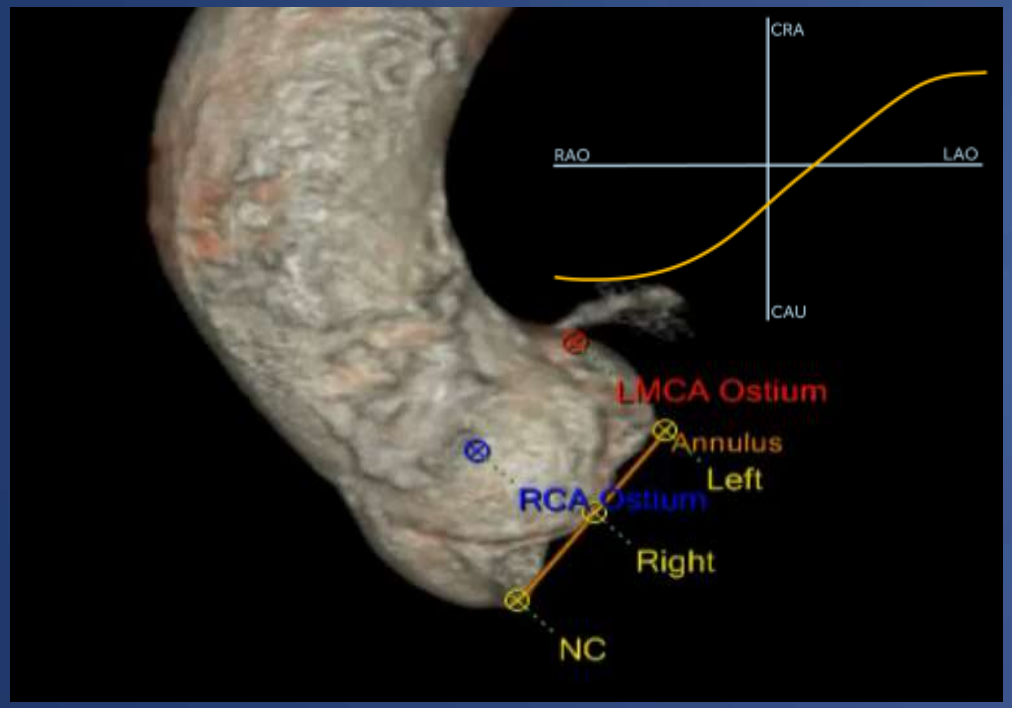
- Centering markers on the cusps is critical for CT determination of overlap imaging projections.



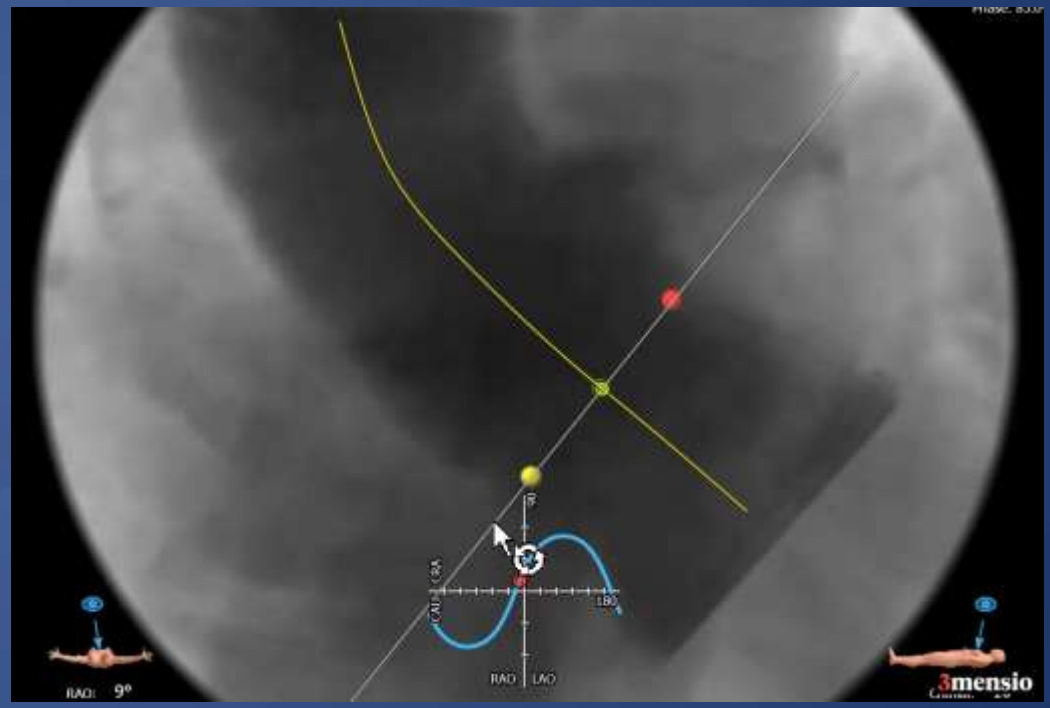


Determine Cusp Overlap Imaging Projections

High quality CT imaging is critical to identify projections along the S-curve.



Rotation along the S-curve allows visualization of the basal annular plane in multiple projections.



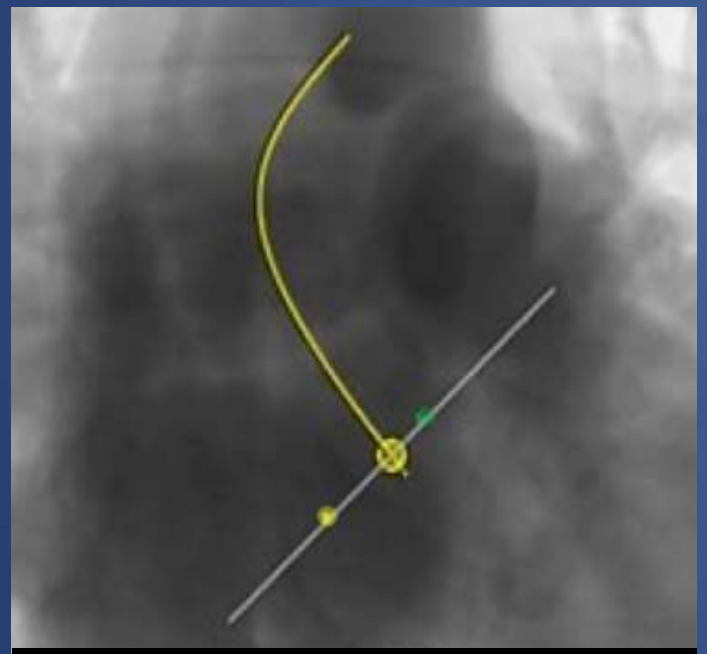
In a long axis view, determine cusp overlap projection by moving along S-curve until RCC and LCC overlap.

Pre-Procedure CT Planning

NEAR OVERLAP VIEW EXAMPLE

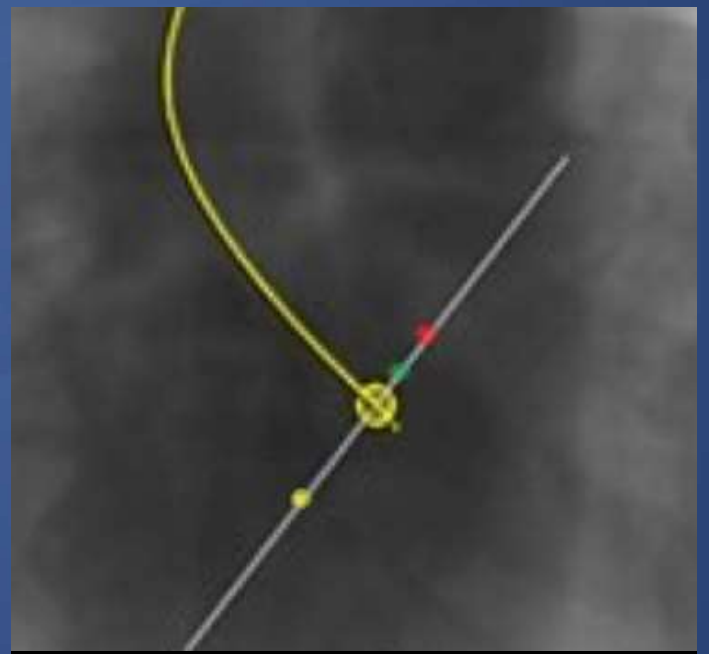
If the cusp overlap imaging projection is unattainable due to patient body habitus and/or equipment limitations, move along S-curve to a near cusp overlap view.

Overlap View



RAO 13˚, Caudal 42˚

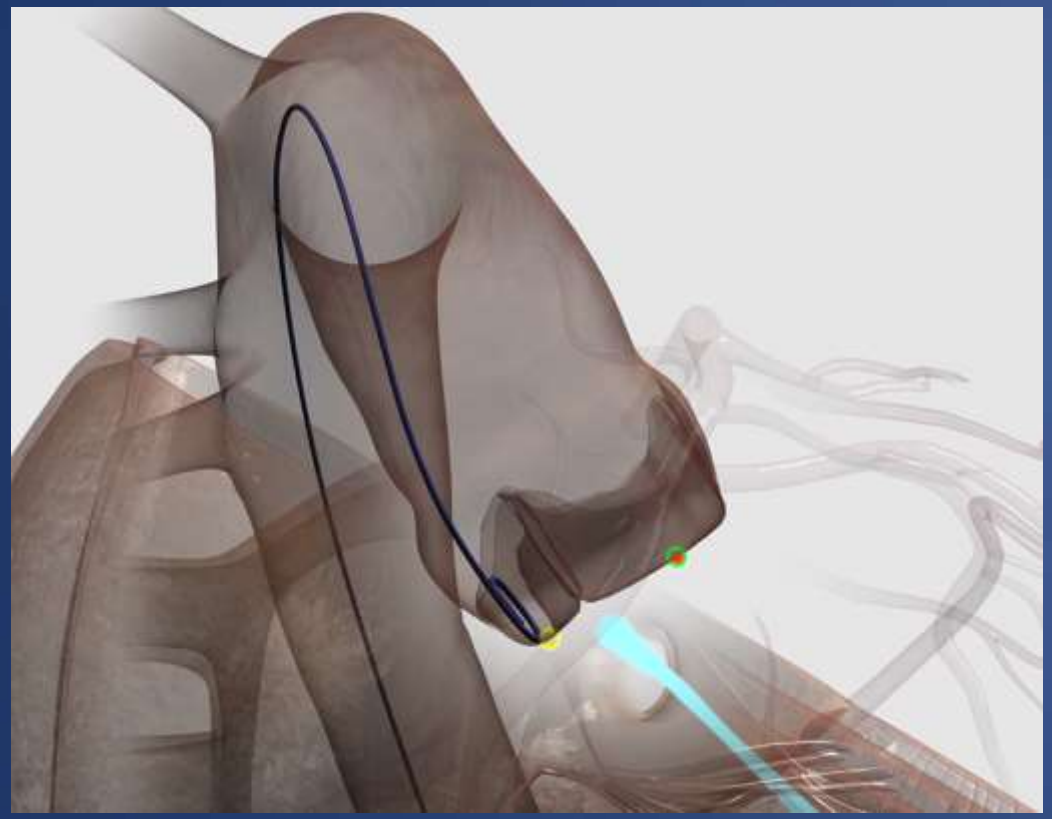
Near Overlap View



LAO 1˚, Caudal 30˚

Assess Depth Accurately at the NCC

The L-R cusp overlap projection isolates the NCC, elongates visualization of the LVOT, and maintains coplanar cusp alignment to provide a more accurate view of TAV depth.



Views which do not maintain alignment of cusps introduce error in perception of TAV depth at the NCC and LCC[1]:

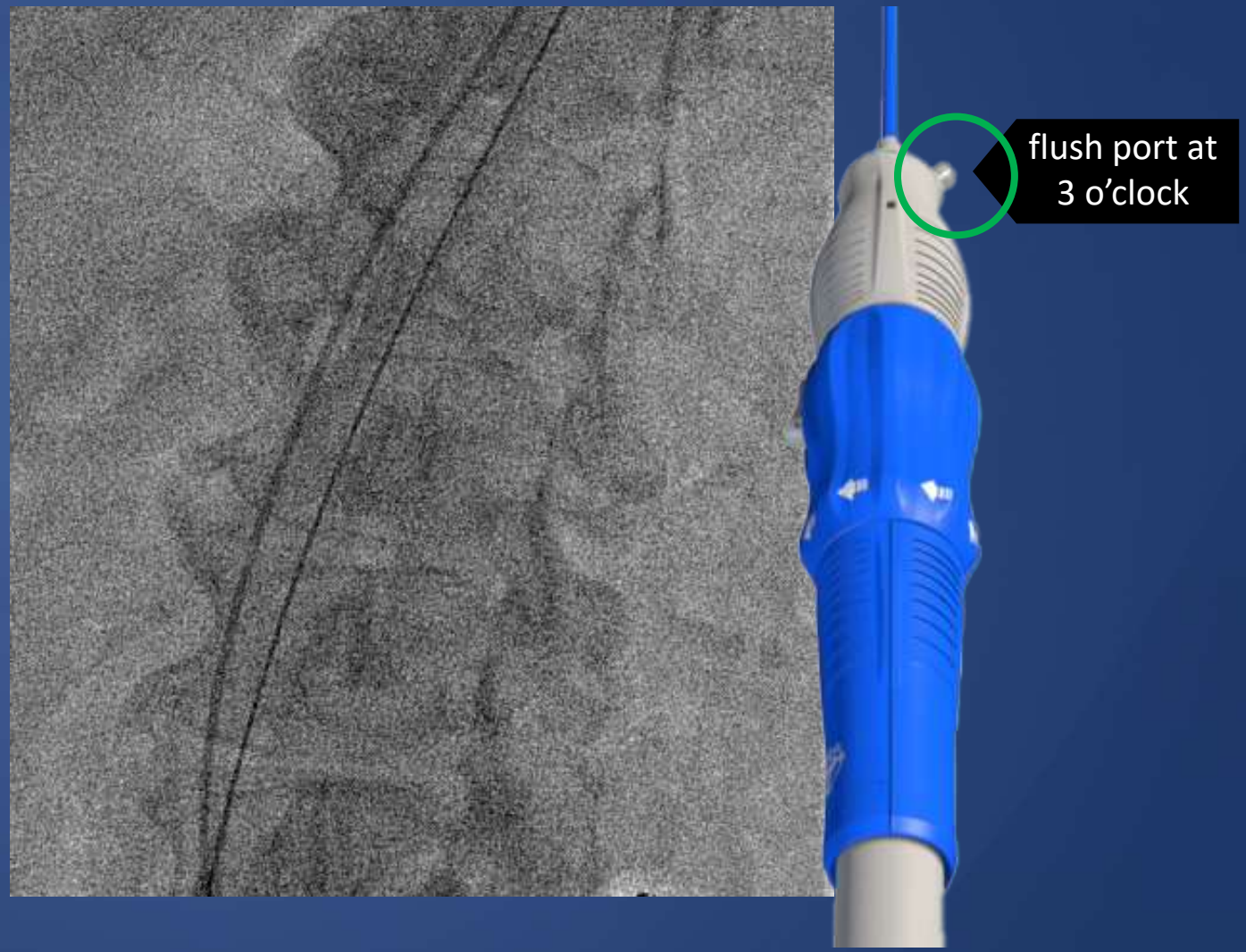
- This error results in TAV appearing higher than actual depth.
- An approximate error of 1 mm in depth is introduced for each 10^{o} movement in the LAO or Caudal directions.

1. Fraser, D. Presented at London Valves, 2019.

Introduce Delivery System

With the InLine Sheath fully forward and the flush port facing away from the operator (oriented at 3 o'clock), load the DCS onto the guidewire and insert into the patient.

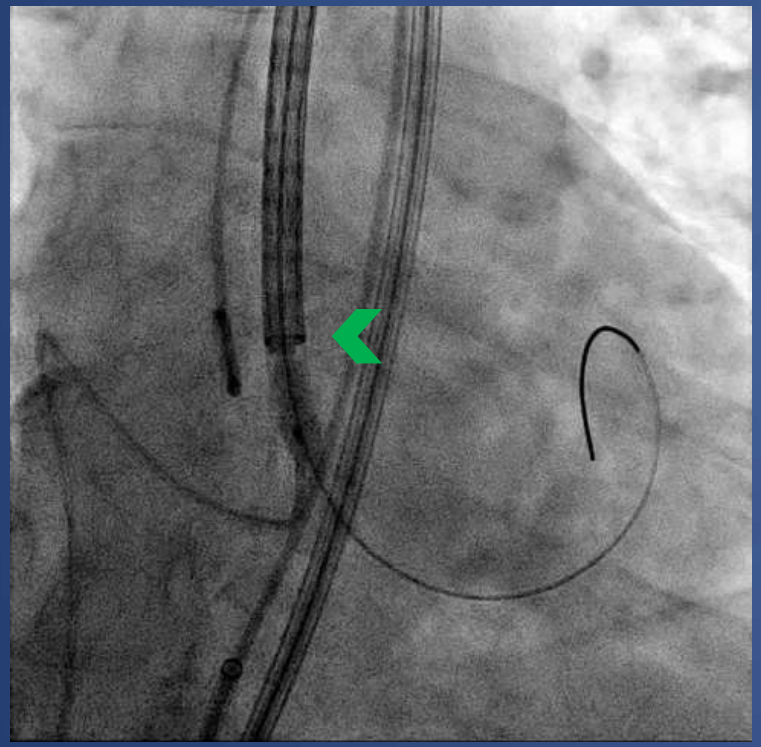
- 3 o'clock flush port orientation is reported to be associated with higher rates of commissural alignment between the TAV and native anatomy.[1]
- Commissural alignment may help facilitate future coronary access.



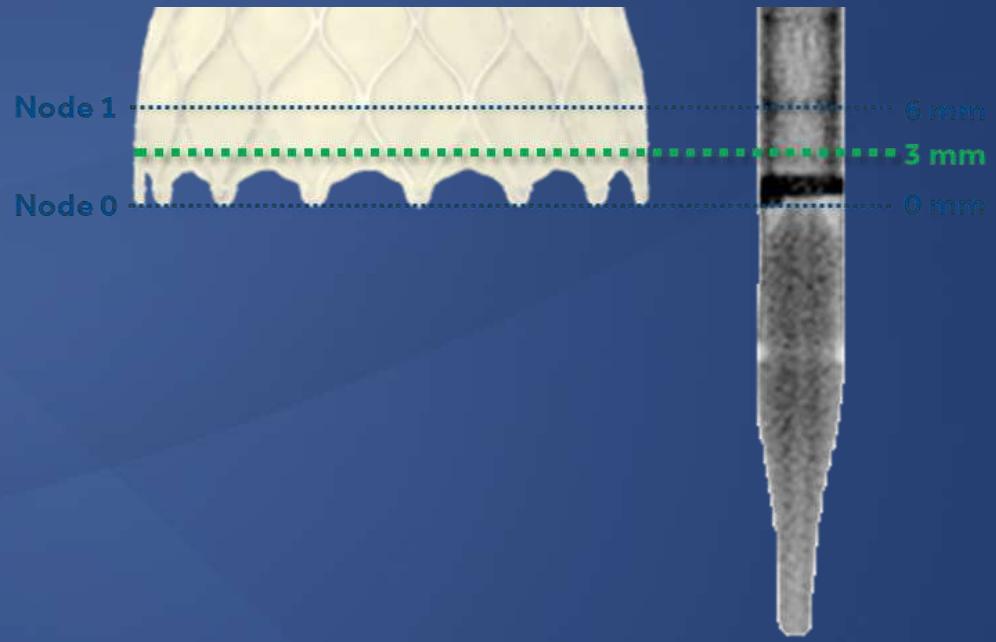
1. Tang et al. JACC: Cardiovascular Interventions, 2020.

Reduce Interaction with Conduction System

More accurate visualization of depth and approaching target depth (3 mm) from above the annulus may reduce potential for conduction disturbances.



Begin Deployment with Radiopaque Marker Band at Mid-Pigtail



3 mm Target Implant Depth

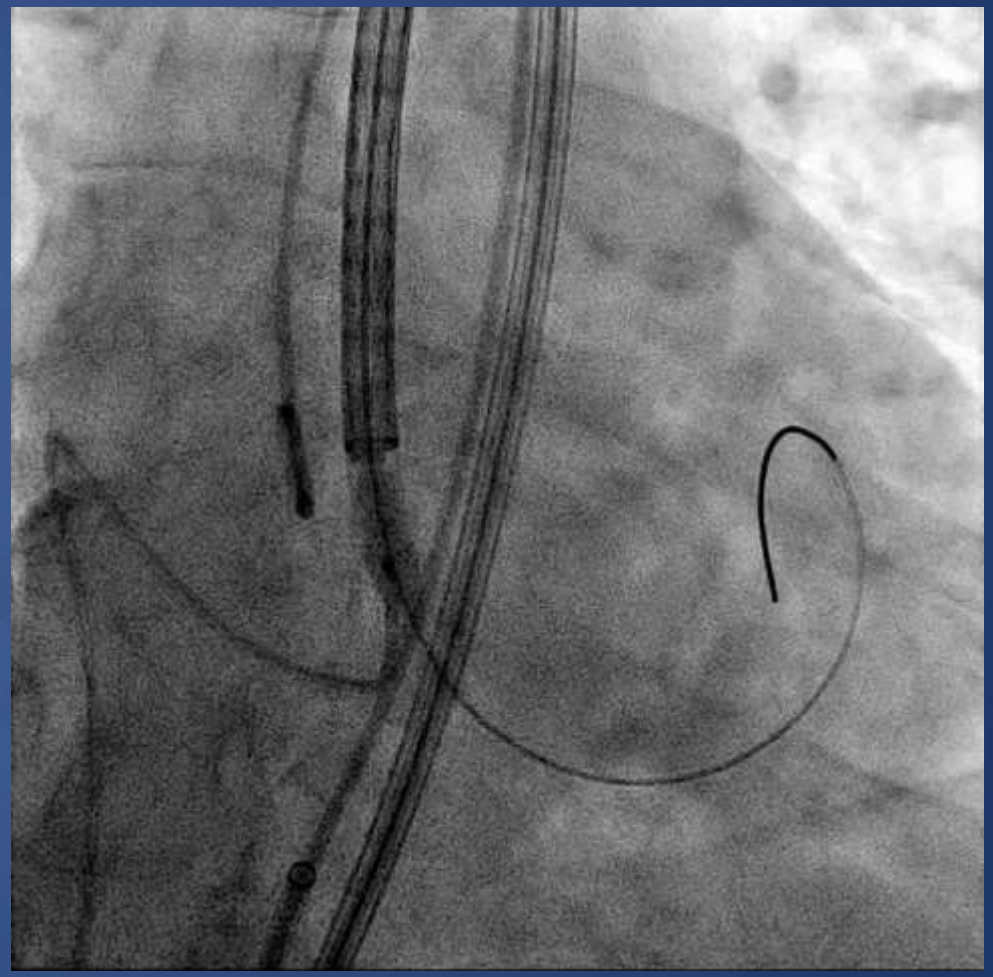
Starting Position

CUSP OVERLAP VIEW

After crossing the arch according to transfemoral best practices, move to the predetermined cusp overlap view.

Confirm placement of pigtail catheter at the bottom of the NCC and position the catheter marker band at the midpoint of pigtail catheter.

- If extreme parallax in catheter marker band is present, consider the following:
  - Adjust to a near overlap view
  - Reposition wire to ensure appropriate placement in non-right commissure
  - Select a more supportive wire

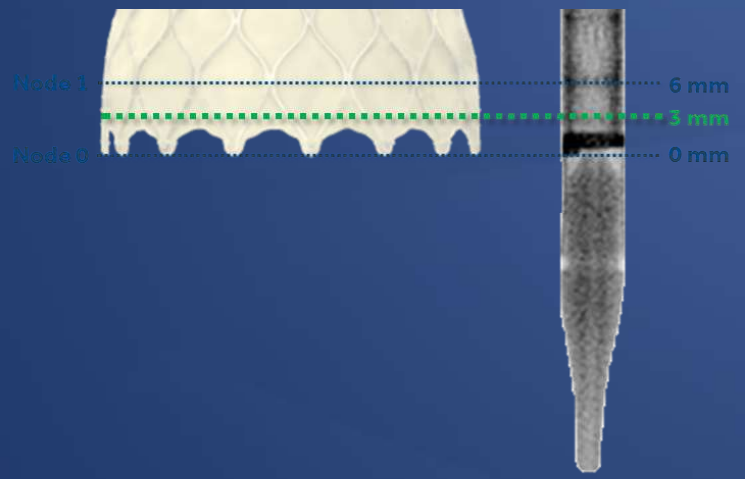


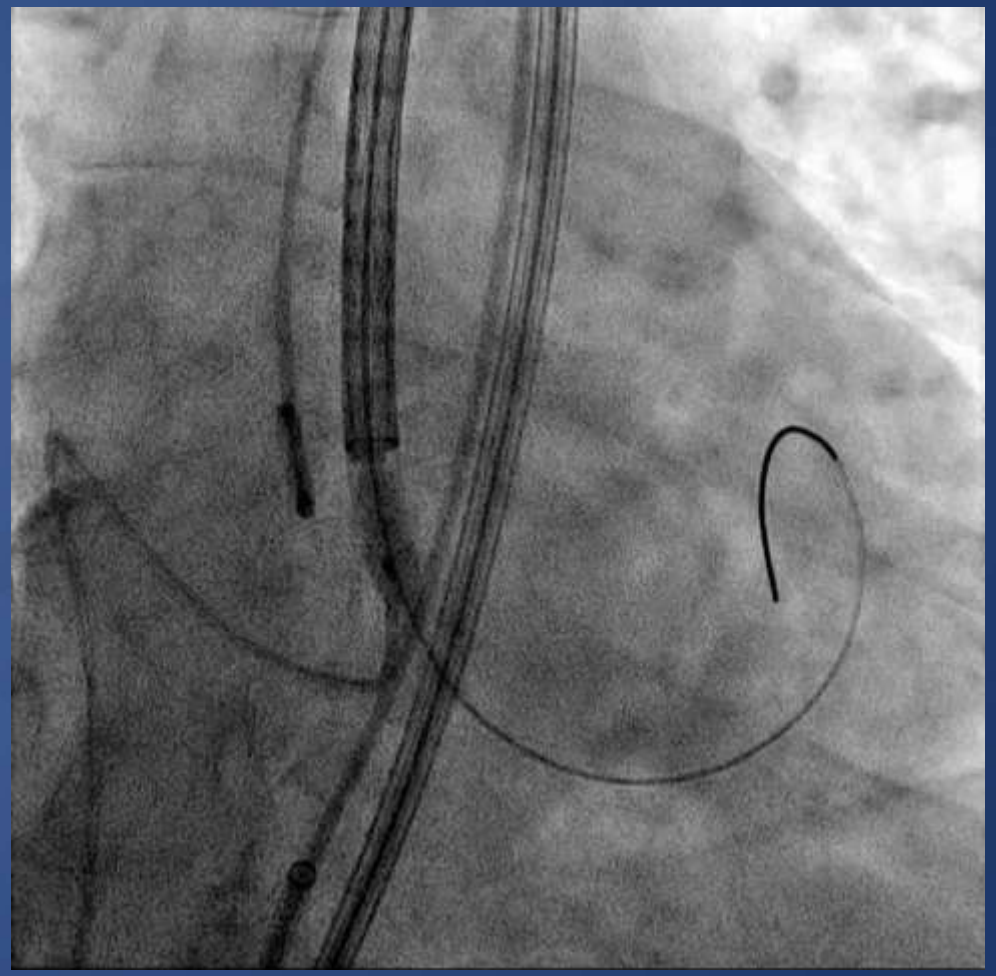
Initial Deployment

ADJUSTMENT TO TARGET IMPLANT DEPTH

Slowly deploy the valve until the marker band reaches the third node of frame.

- Use small movements (¼ turns) to facilitate slow deployment
- Approach target depth (3 mm) from a supra-annular starting position to allow valve to descend to target depth
  - This method is intended to minimize interaction below annulus to reduce risk of conduction abnormality





Pacing Considerations

- **Consider using pacing to help increase valve stability by:**
  - Stabilizing hemodynamics.
  - Minimizing potential for late movement due to ectopy or respiration.

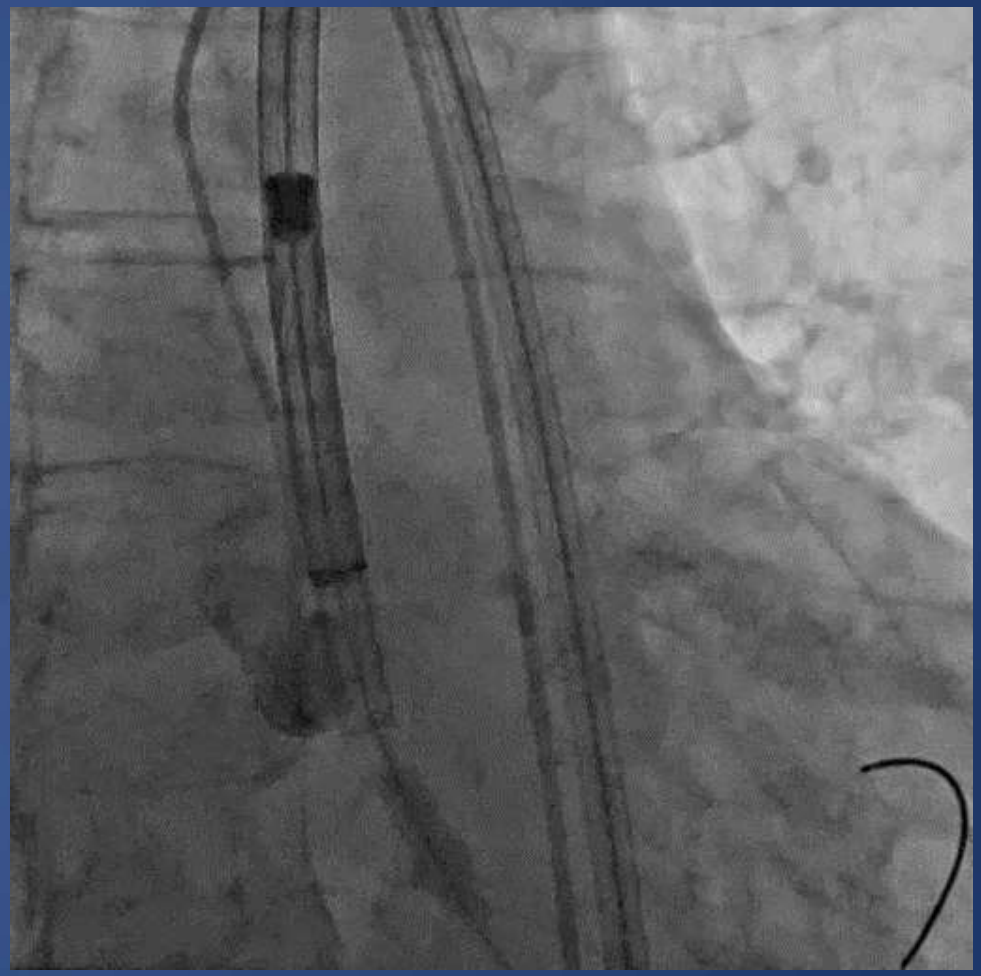
- **Steps**:

- Begin pacing when marker band is at 3rd node (prior to annular contact).

- Start pacing at 120 bpm and adjust, in consideration of individual patient factors, to achieve desired systolic pressure.

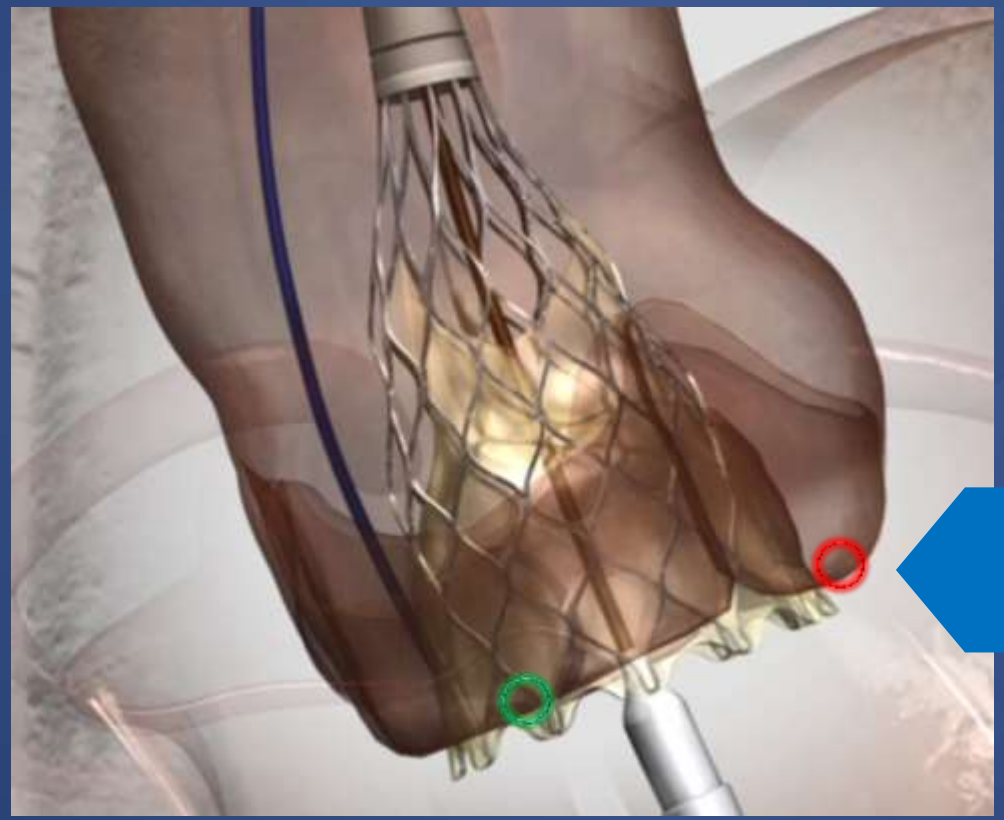
- Rapidly deploy from annular contact to before the point of no recapture as unexpanded bioprosthesis temporarily obstructs cardiac output.

- Discontinue pacing immediately before reaching the point of no recapture.
  - Consider discontinuation of pacing by stepping the rate down incrementally.



Trust the Cusp Overlap View for NCC and Verify LCC Depth in the LAO View

Moving to an LAO view before the point of no recapture allows separation of the LCC to confirm depth and inform the decision to deploy or recapture the TAV.



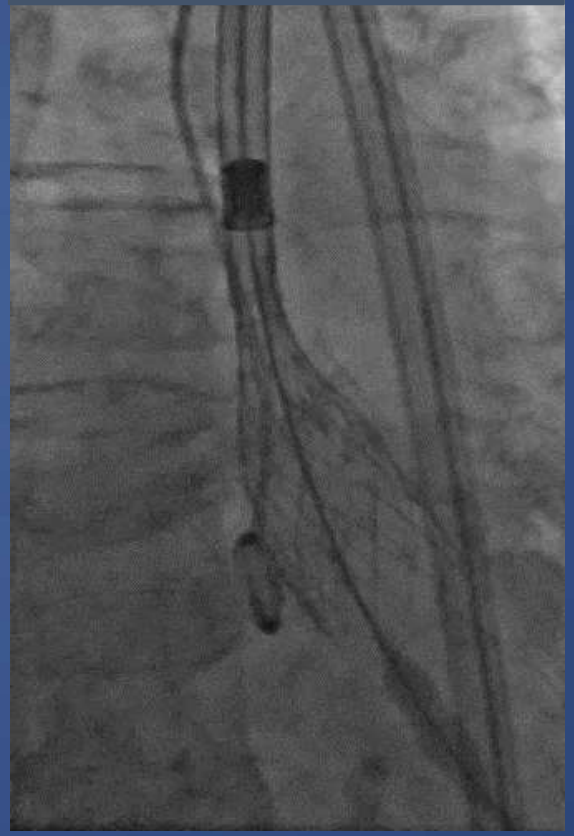
Confirm TAV depth at LCC in the LAO view

Move to LAO View

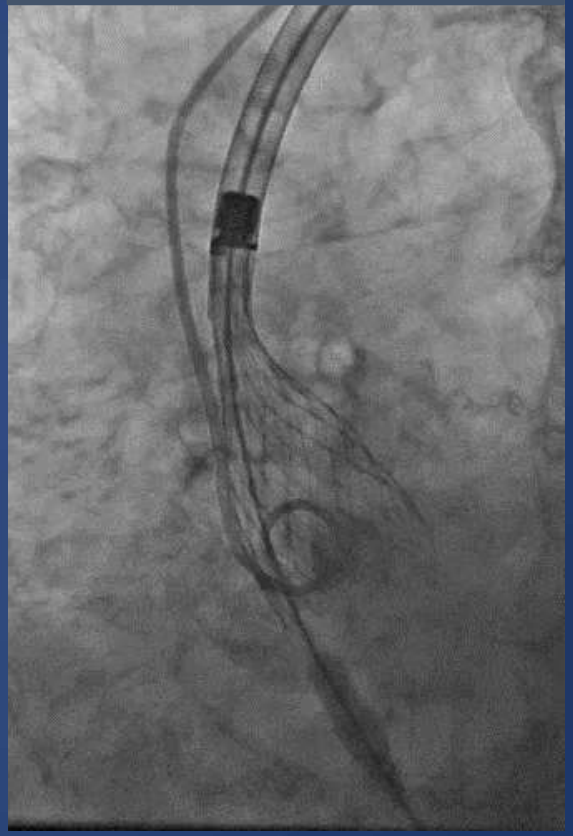
CONFIRM DEPTH AND PERFORMANCE

- **Move to a 3 cusp coplanar view and then roll LAO (no greater than 25˚) until aortic arch is open and parallax at the inflow is minimized.**
  - Remove any remaining parallax at inflow by moving caudal
- Assess depth at LCC
- Confirm valve performance:
  - Assess hemodynamics and prosthetic regurgitation
  - Confirm coronary perfusion
  - Determine whether to deploy or recapture

Cusp Overlap View



LAO View



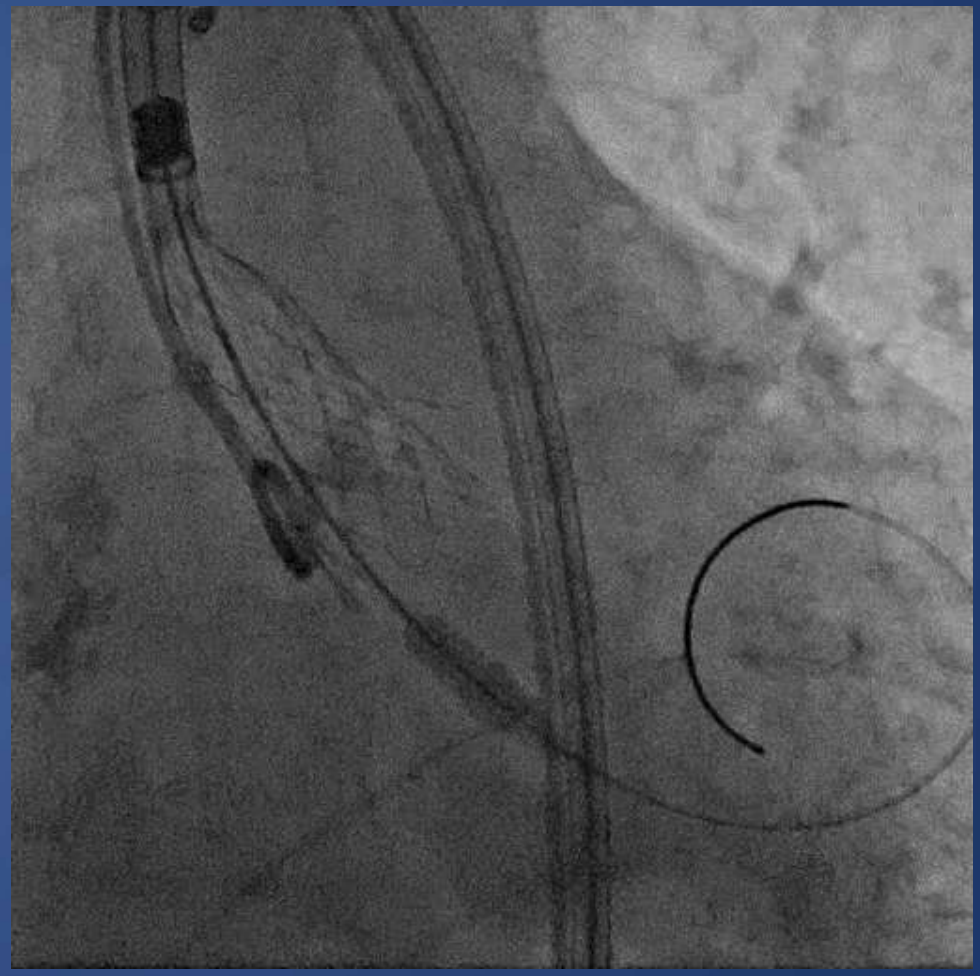
Recapture Considerations

Just before the point of no recapture, assess valve position and depth; consider recapturing the TAV if depth is < 1 mm or > 5 mm at the NCC.

- Depth < 1 mm may contribute to an increased risk of valve migration upon release.
- Depth > 5 mm may contribute to an increased risk of conduction disturbances which may require a permanent pacemaker.

The valve can be partially or fully recaptured up to three times at any point before the point of no recapture:

- First two attempts to reposition and redeploy the valve.
- Third attempt must be a complete recapture and retrieval from patient.



Note: the valve will occlude cardiac output between 2/3 to 1/3 recapture.

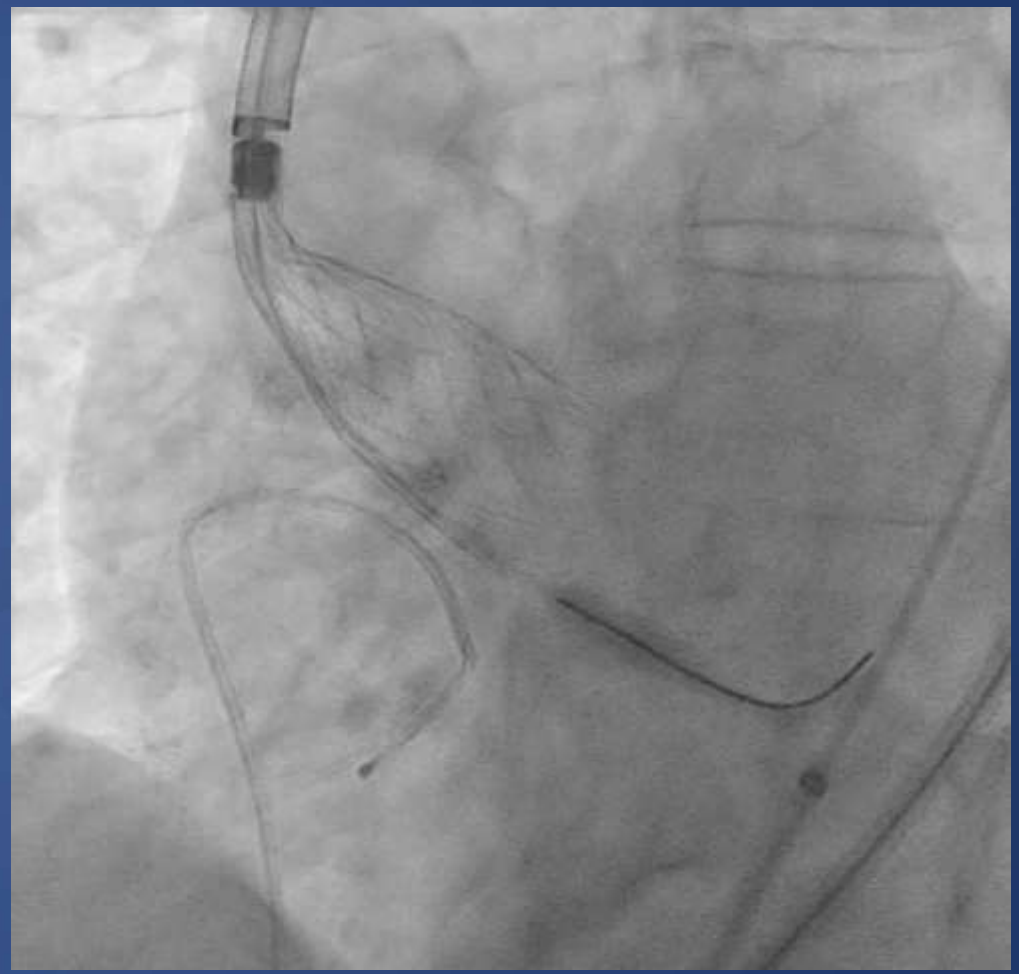
Deployment

PREPARING FOR FULL RELEASE

- After confirming valve position and performance, release tension, apply forward pressure to centralize delivery system in aorta, and pull guidewire back from apex.

- Remove pigtail from NCC.

- Very slowly deploy as outflow region leaves capsule and paddles release.
  - Use ¼ turns and pauses to minimize any potential movement upon release.
  - This final phase of deployment should generally be completed over 30 seconds.



CoreValve

Self-Expanding Frame

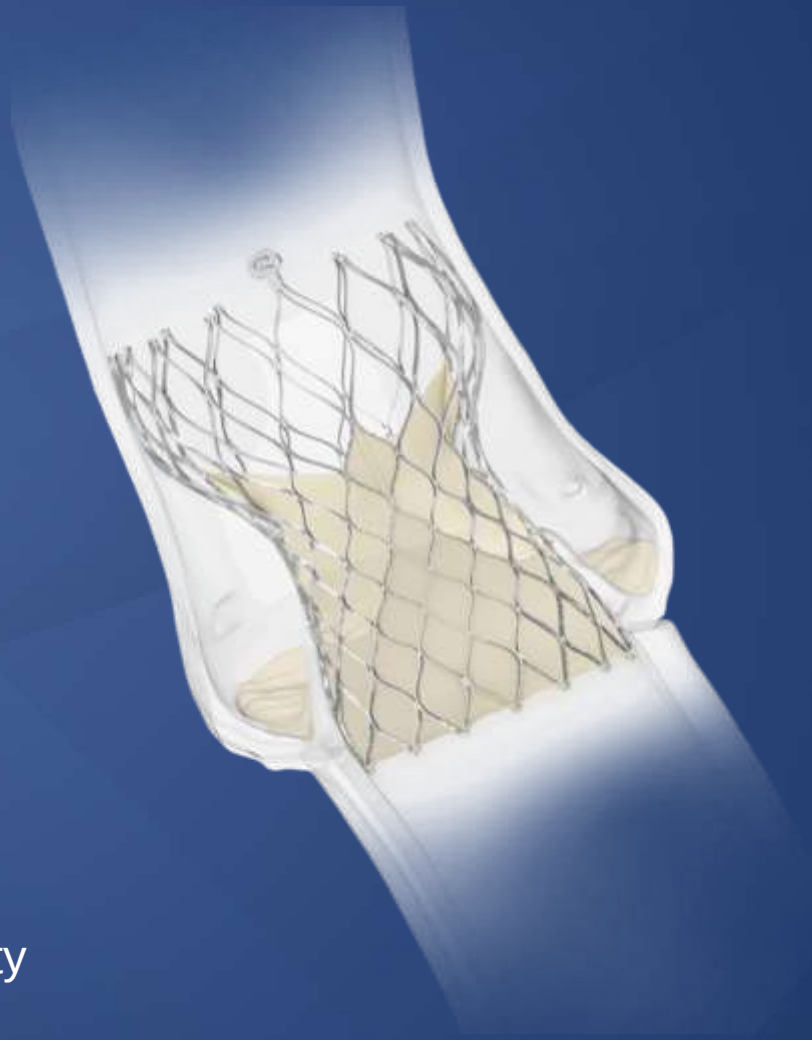
- Conforms and seals to the annulus
- The foundation for recapturability

Supra Annular Valve Design

- Maximize flow and optimize coaptation

Porcine Pericardial Tissue

- Thinness for low profile delivery
- Strength and pliability for long-term durability



CoreValve Evolut R System

Recapturable valve and delivery catheter with loading system

Catheter Delivery System

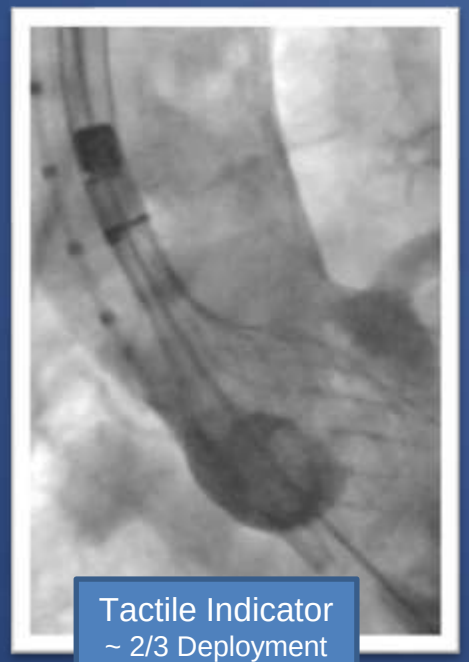
14Fr-equivalent profile

Loading System

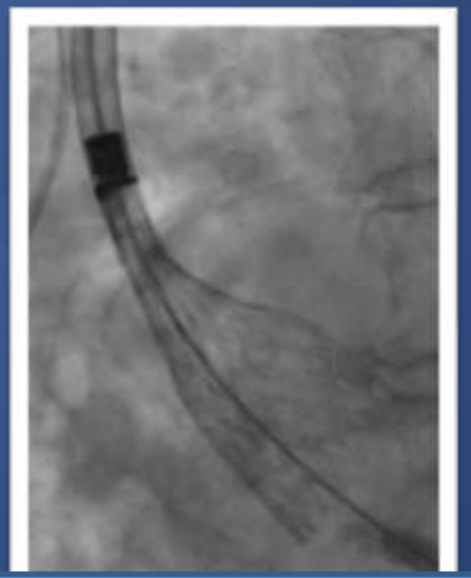
Transcatheter Valve

Evolut R
Recapture and Reposition

EnVeo R DCS provides option to *recapture and reposition up to three times* before reaching the 'Point of No Recapture'*



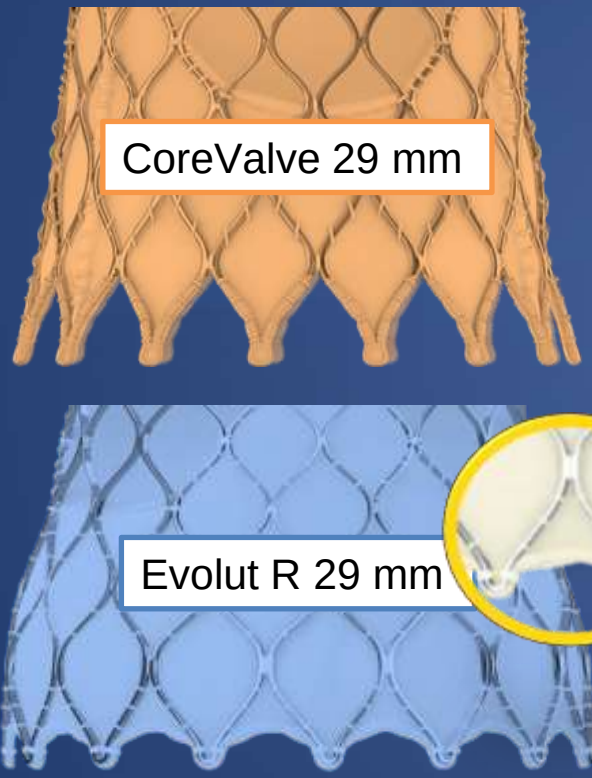
Tactile Indicator
~ 2/3 Deployment



Just Prior to Point of No Recapture
~ 80% Deployment*

* Up to 80% deployment

Evolut R
Enhanced Sealing

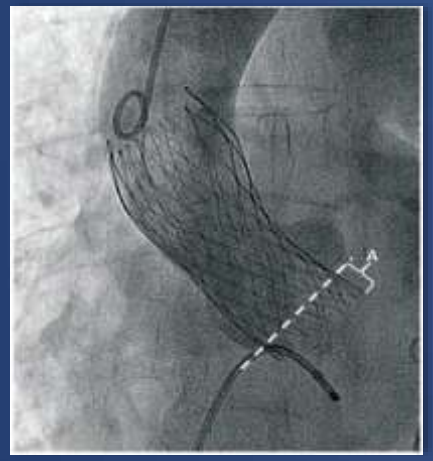


Enhanced Sealing with a More Conformable Frame *

1. Increased Oversizing
2. More Consistent Radial Force
3. Extended Sealing Skirt

Note: images may not be to exact scale and are for illustration purposes only.
*CoreValve Evolut R 26 and 29 mm only

Design Goals For Evolut R



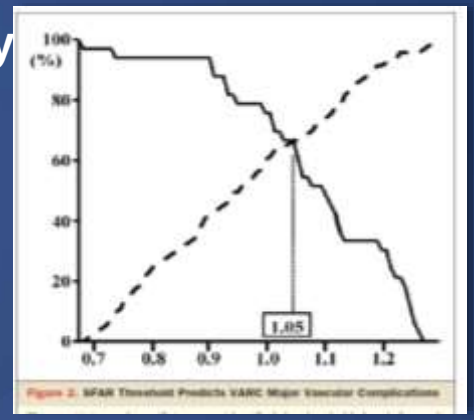
(TcheTche, et. al. – EuroIntervention 2012)

1. **Low Sheath OD to Femoral Artery Ratio (SFAR)**
   Reduces risk of major vascular complications and improves access

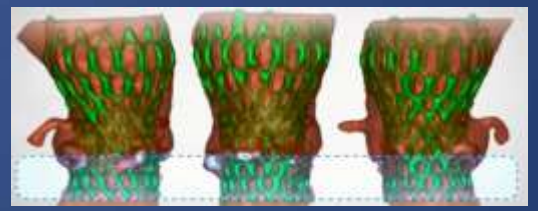
2. **Positioning Accuracy** Key to achieving superior clinical outcomes, including PVL performance and conduction disturbances

3. **Annular sealing**
   Reduces paravalvular leak

4. **Ease-of-use**



(Hayashida K., Lefevre T., Chevalier B.; et al. Transfemoral Aortic Valve Implantation; New Criteria to Predict Vascular Complications, J Am Coll Cardiol Intv 4 2011 851-858)



CT images courtesy of Dr. Piazza and Prof. Lange, German Heart Center, Munich Germany

Evolut R : broad coverage of size

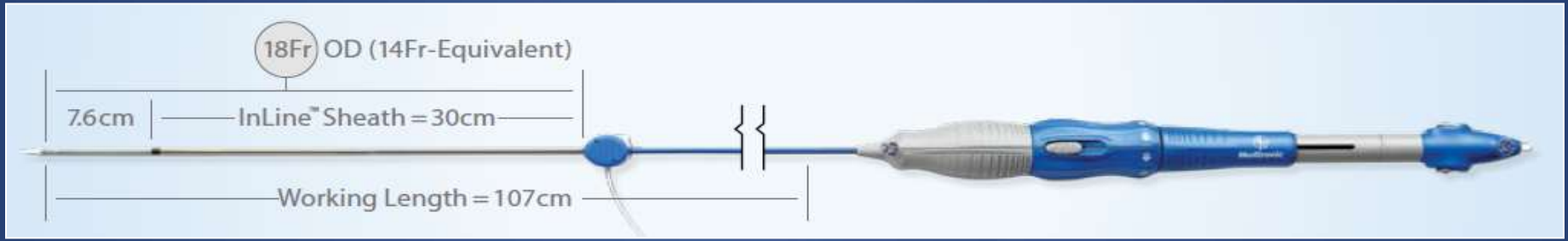
Indicated Size Range

Evolut R 23, 26, 29 mm
CE and FDA Approved

Evolut R 34 mm
Received IDA Approval

Patient Annulus Diameter Range (mm)

EnVeo R Delivery Catheter Dimensions



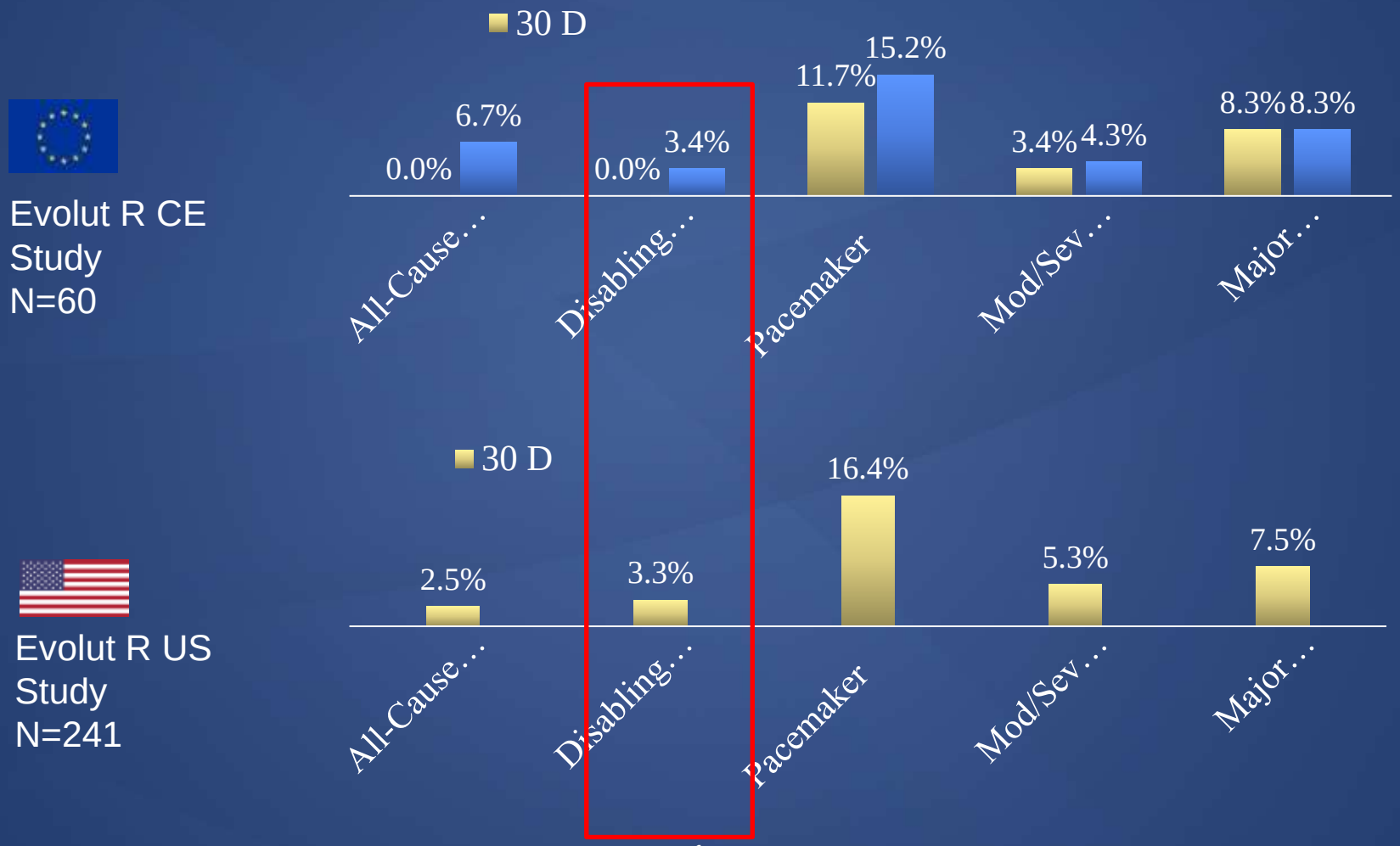
Lowest Delivery Profile

True 14Fr system with 5mm vessel indication

Sheath size comparison (Evolut R vs Sapien3)

Evolut R Clinical Evidence : low risk of stroke

Medtronic-Sponsored Studies



[1]Manoharan, et al., J Am Coll Cardiol Intv 2015; 8: 1359-67;
[2]Manoharan, et al., presented at TCT 2015;
[3]Williams, et al., presented at ACC 2016;

Evolut R :

Wide Orifice Area With Supra-Annular Valve Design

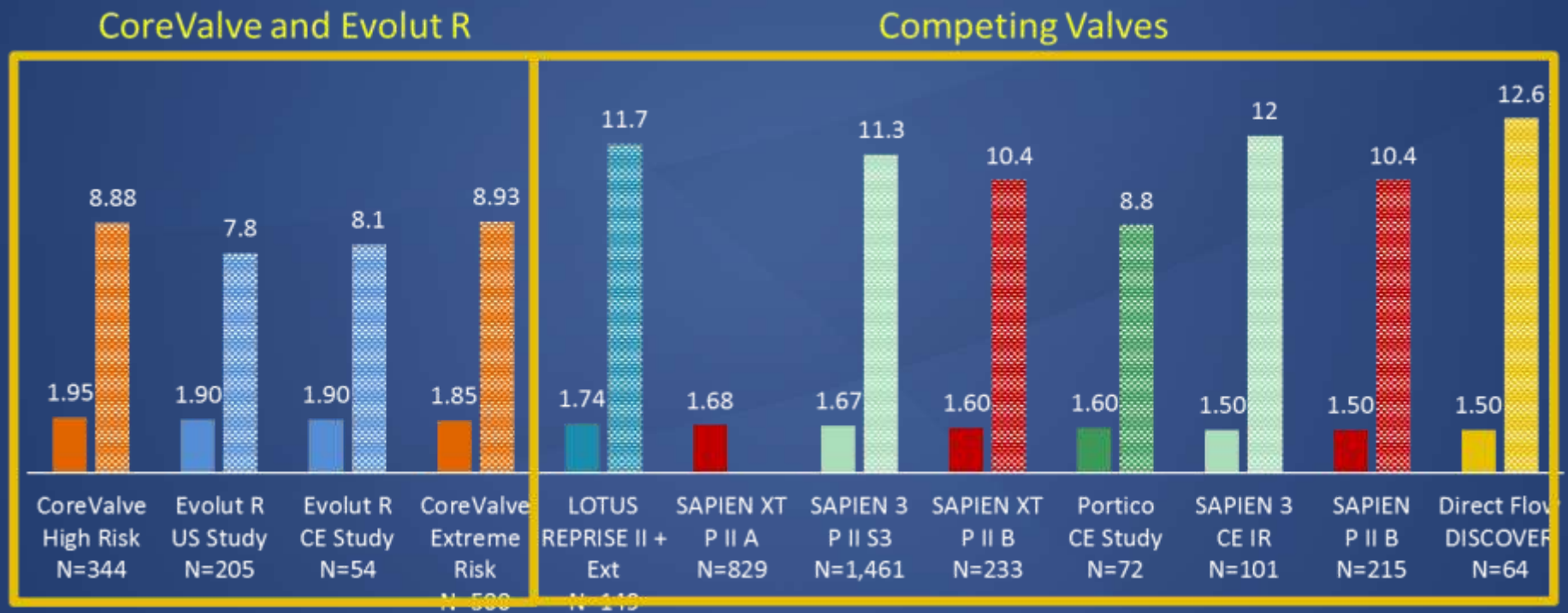
Evolut R

Sapien 3

Lotus

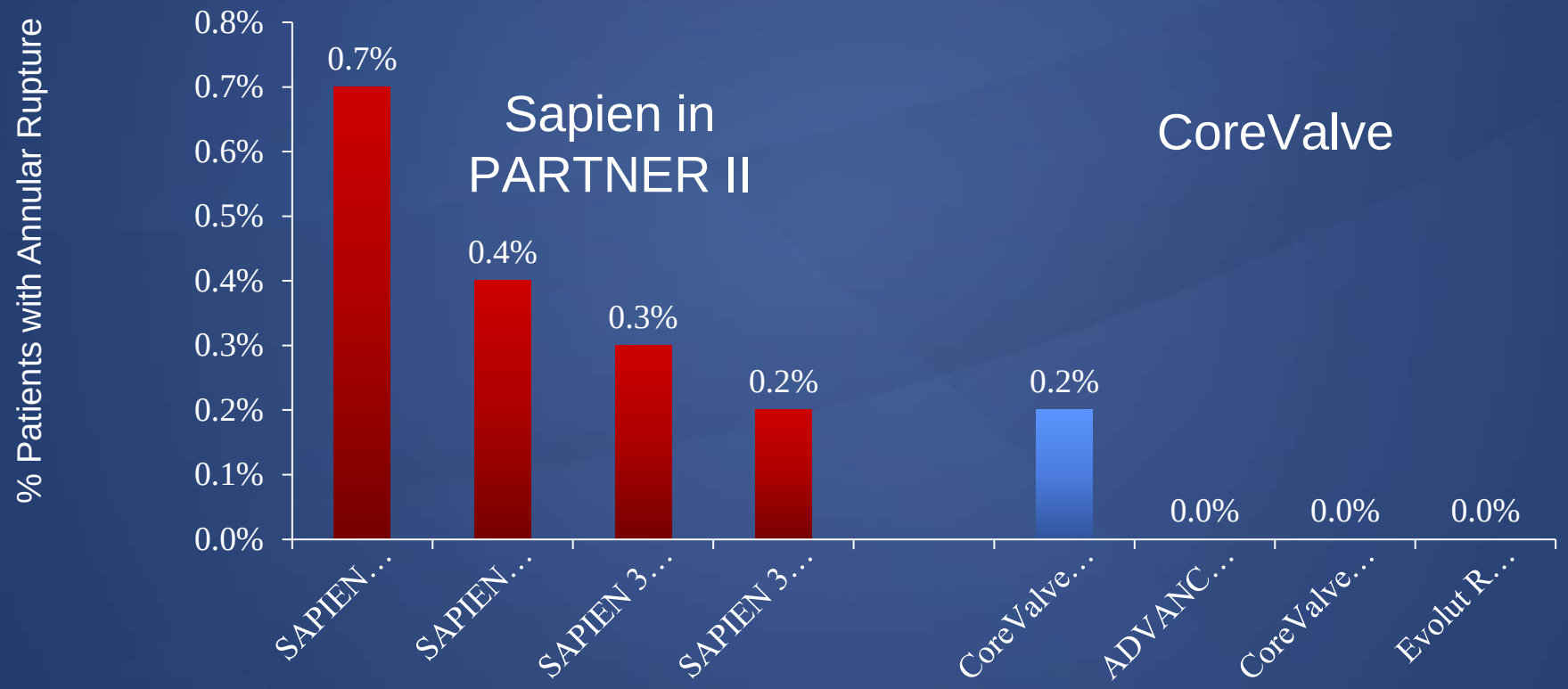
Hemodynamics : best d/t wide orifice area

EOA (cm^2) and Mean Gradient (mm Hg) at 30 Days



Evolut R : Annular Rupture is Rare

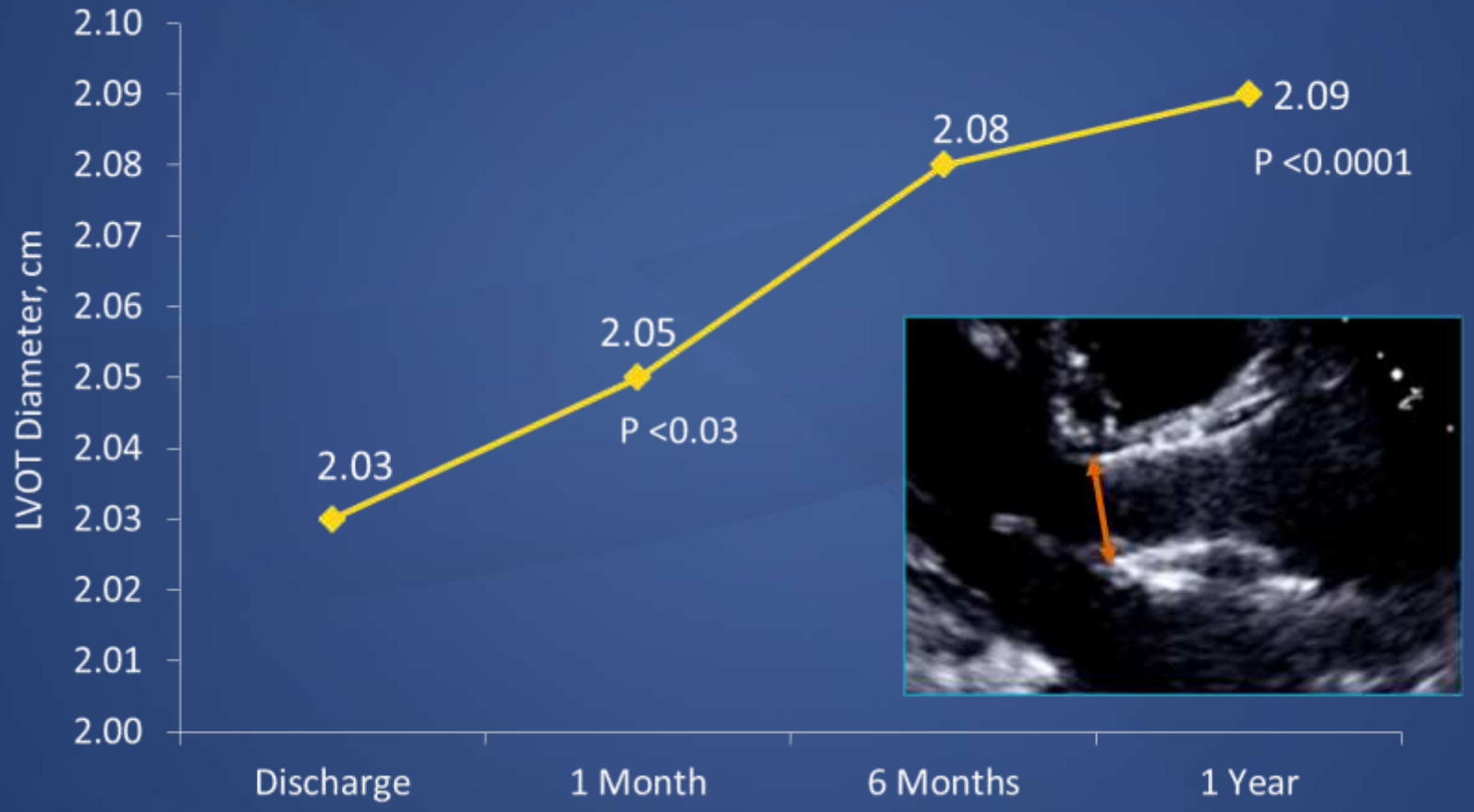
Annular rupture is mainly associated with the inflation of a balloon, either during valve deployment or pre- or post-dilation



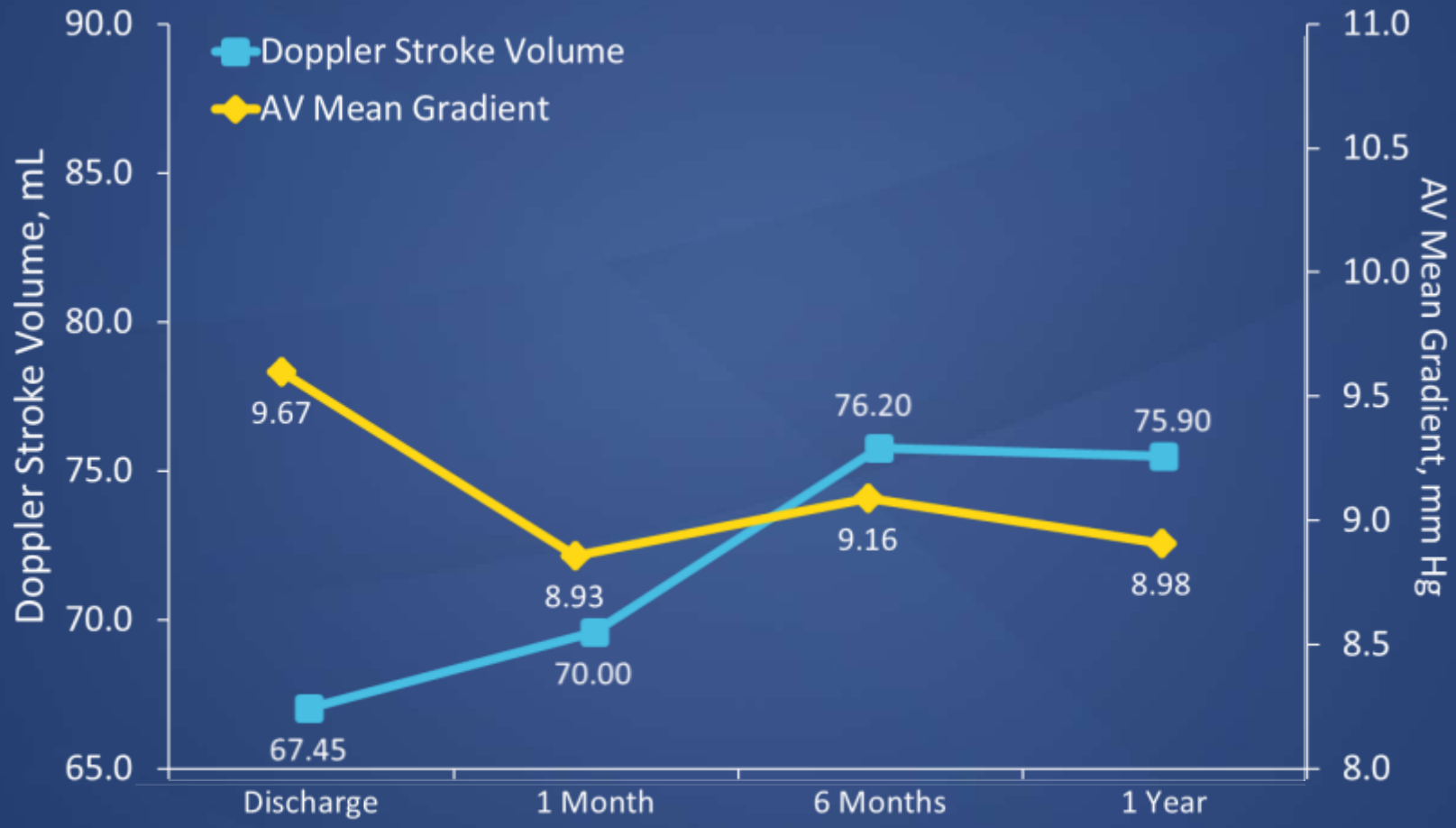
[1]Leon, et. al. presented at ACC 2013; [2]Kodali, et al., presented at ACC 2015; [3]Popma, et al., J Am Coll Cardiol 2014; 63: 1972-81; [4]Linke, et al. , Eur Heart J 2014; 35: 2672-84; [5]Adams, et al., N Engl J Med 2014; 370: 1790-8; [6]Meredith, et. al. presented at EuroPCR 2015

Evidence of Continued Outward Expansion

LVOT Diameter Outer to Outer Edge

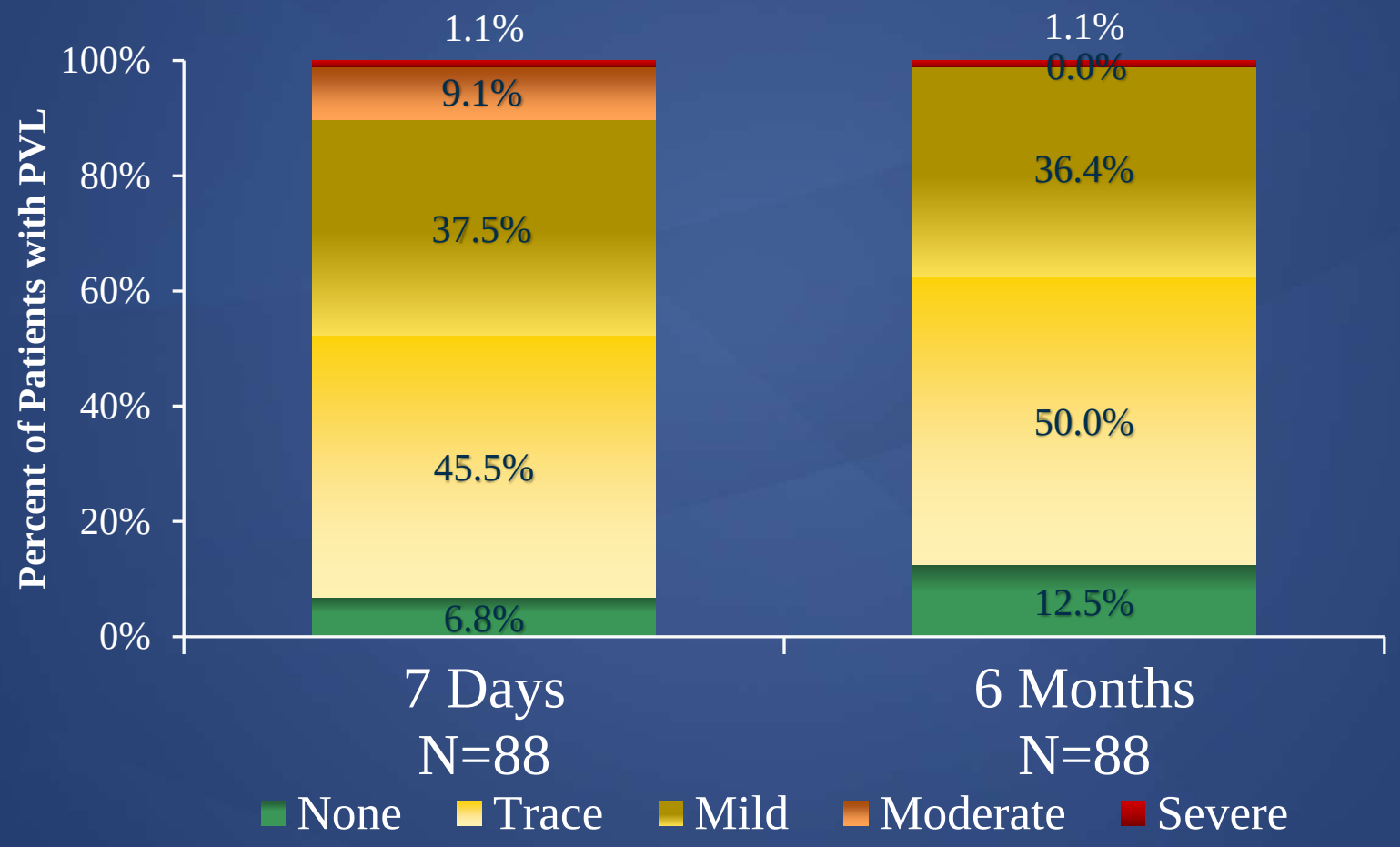


Continued Outward Expansion
Leads to Reduction in AV Gradient



Continued Outward Expansion
Leads to Regression of PVL with Time | ADVANCE II Study

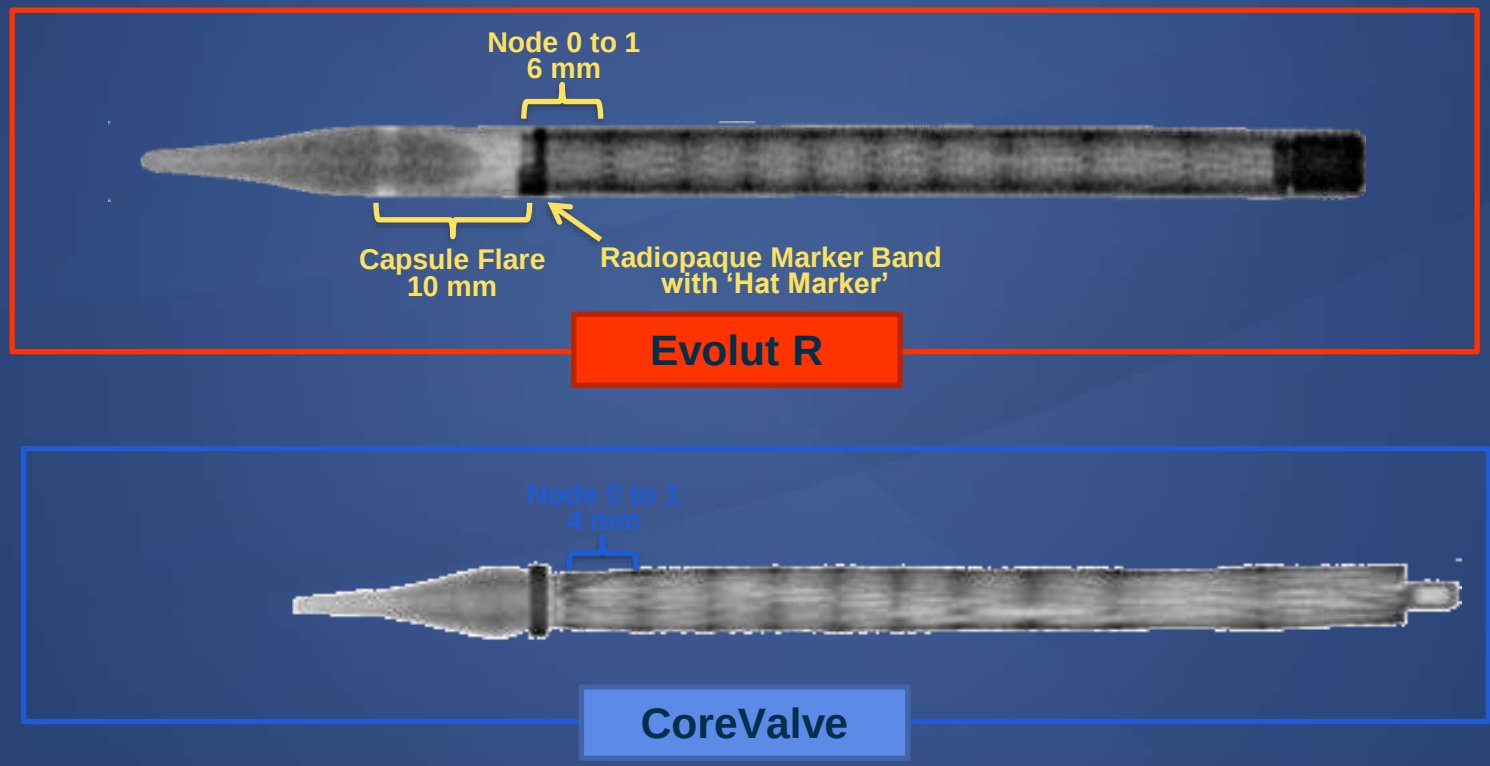
Paired data show >mild PVL decreased significantly from day 7 to 6 months (p=0.005†)



†McNemar's test on paired data

CoreValve ADVANCE II Study

Loaded Capsule under Fluoroscopy

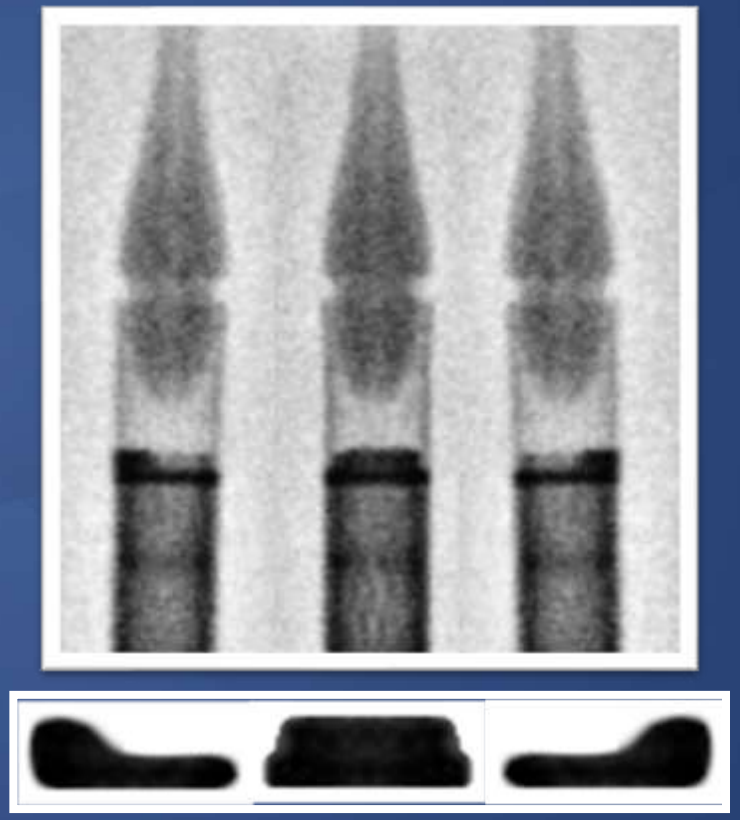


Note: Measurements provided are approximate based on engineering specifications.

Marker Band with Hat Marker

The hat marker is a wider portion of radiopaque marker band extending approximately 1/3 the circumference of the marker band

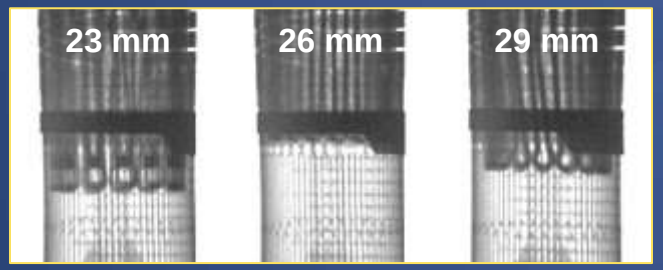
- Resembles a hat when viewed under fluoroscopy
- Used to assess delivery system orientation

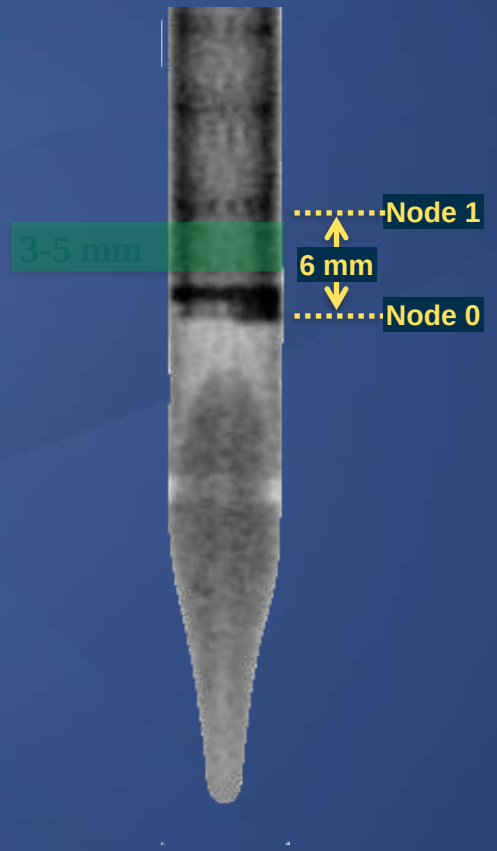


Evolut R Target Implant Depth

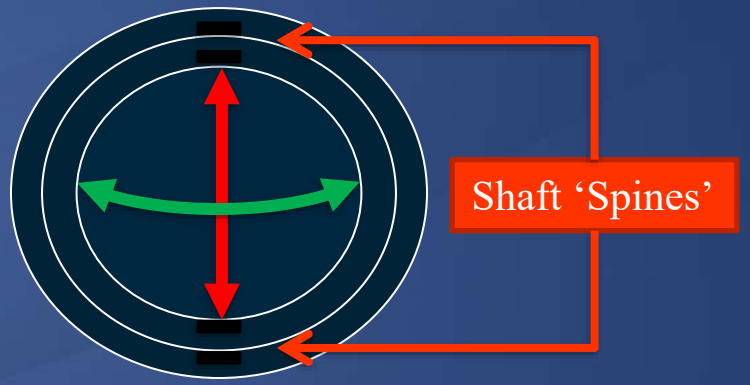
Target implant depth is **3 - 5 mm**

- Midway between node 0 (inflow edge of frame) and node 1 to just below node 1
- Note: due to minor valve frame length differenc es, ensure to assess valve position from frame inflow (node 0) and not the edge of the marker band:





Positioning Accuracy: 1:1 Response

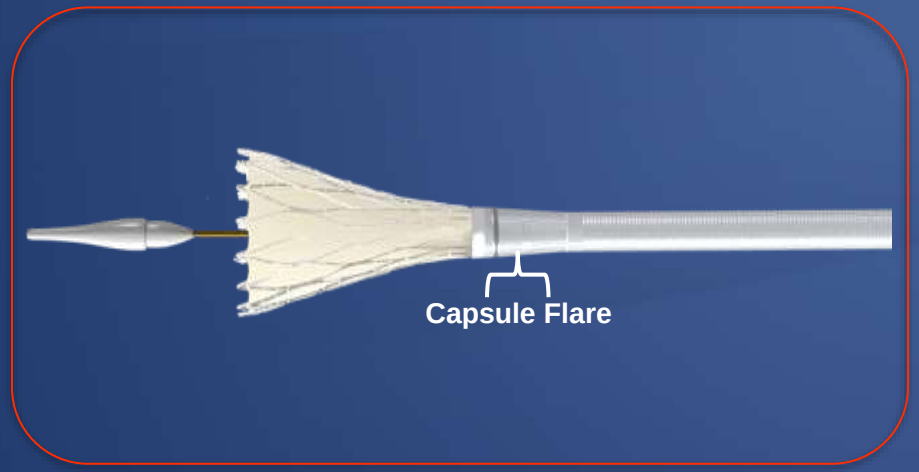


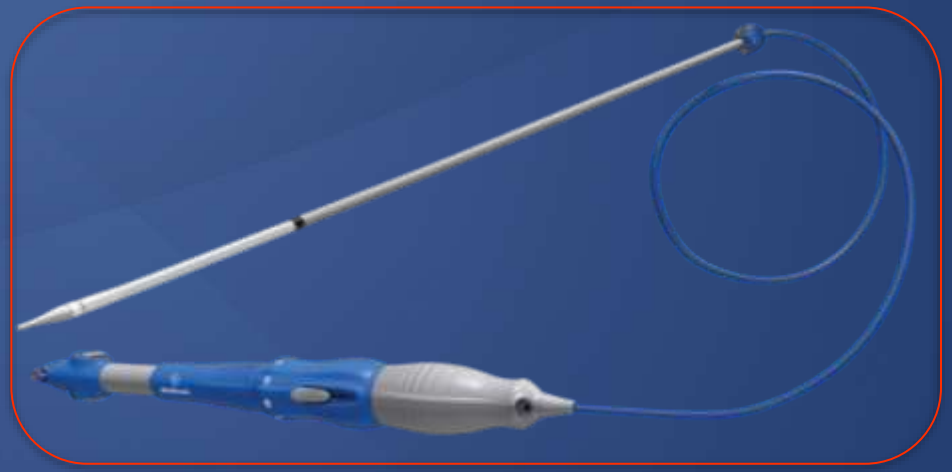
Cross section of catheter shaft
(excluding the stability layer)

Catheter shaft ‘spines’ provide stability to reduce stretching or compr essing of shaft to enable 1:1 Response

Positioning Accuracy: Self-Centering

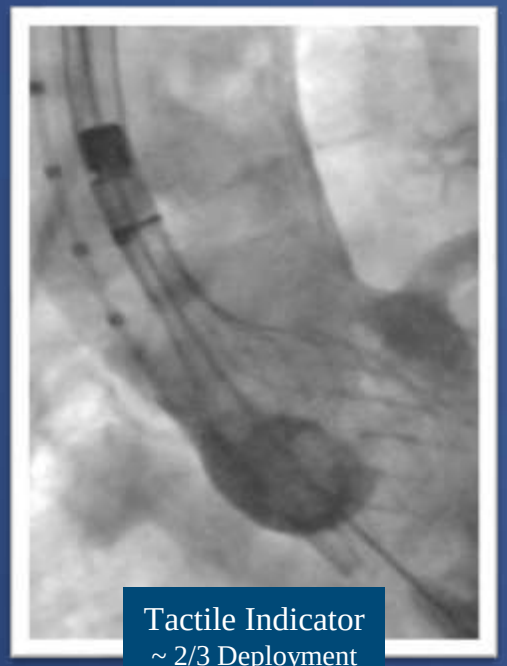
EnVeo R's Capsule flare and flexible catheter design enable uniform and controlled valve expansion and self-centering of the valve in the annulus



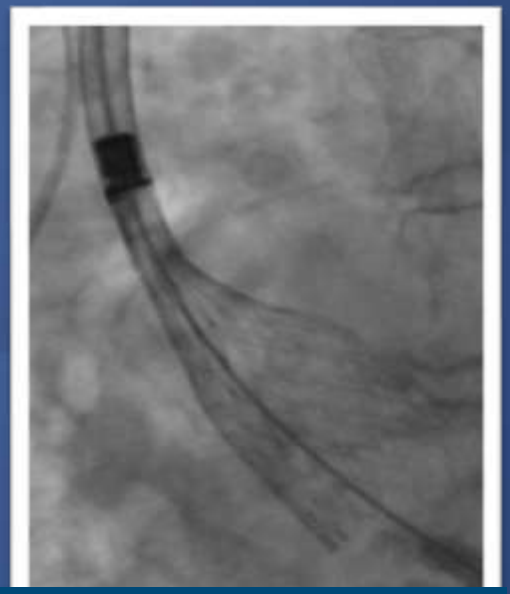


Positioning Accuracy: Ability to Recapture and Reposition

EnVeo R provides option to recapture and reposition up to three times before reaching the 'Point of No Recapture'*



Tactile Indicator
~ 2/3 Deployment

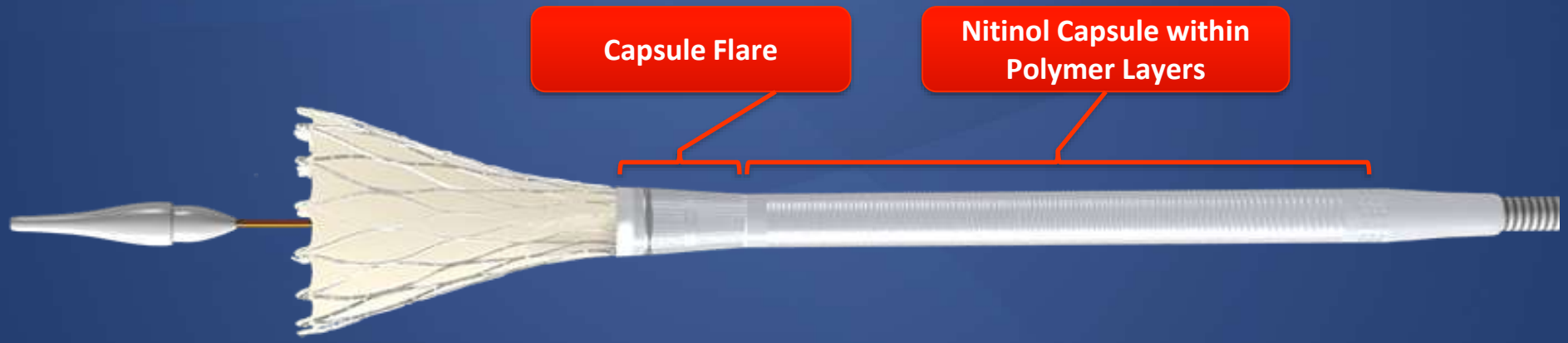


Just Prior to Point of No Recapture
~ 80% Deployment*

* Up to 80% deployment

Positioning Accuracy: Ability to Recapture and Reposition

Laser-cut Nitinol capsule within two polymer layers provides structural suppor t necessary to resheath partially deployed valve.

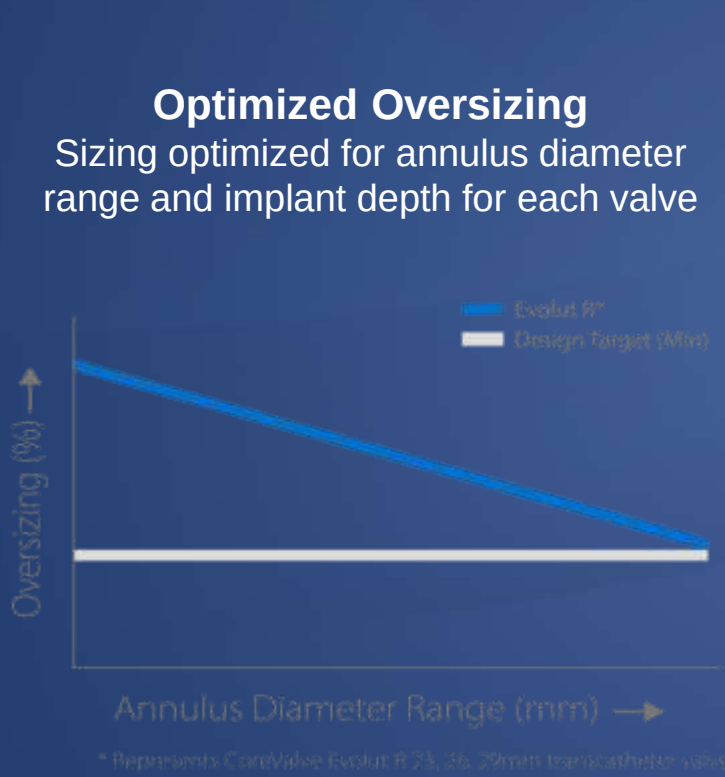


Enhanced Sealing: Optimized Oversizing, Consistent Radial Force, and Extended Sealing Skirt[1]

For Exceptional Valve Performance and Reduced Significant PVL[2]

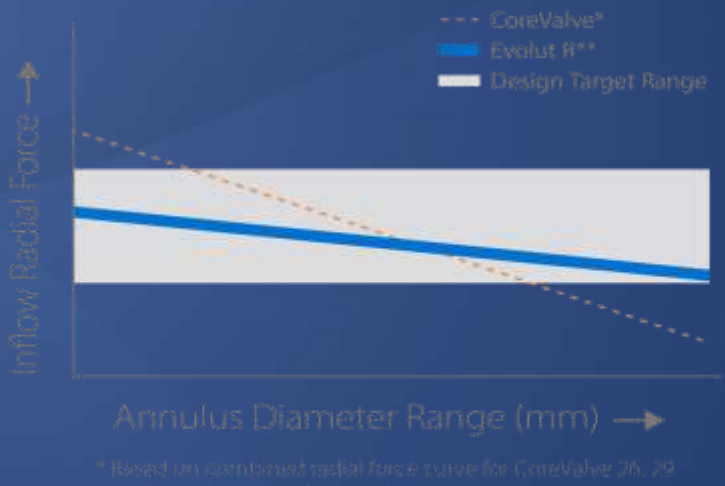
Optimized Oversizing

Sizing optimized for annulus diameter range and implant depth for each valve



Consistent radial force

Contributes to improved sealing across indicated annulus range for each valve



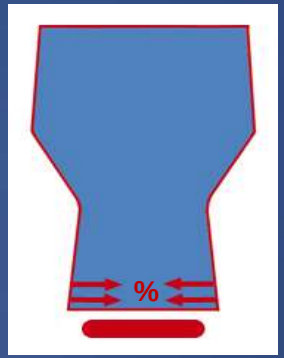
1. Available on 26 and 29 mm sizes
2. Medtronic data on file. 23R comparison of CoreValve to CoreValve Evolut. Significant PVL defined as ≥ moderate PVL.

Optimized Oversizing

Oversizing

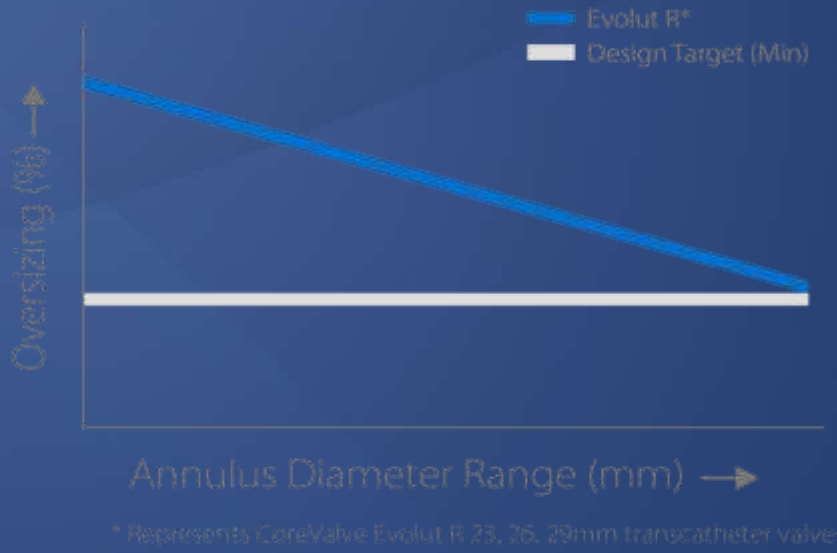
- The size of the bioprosthesis inflow dia meter relative to the native annulus:

$$Oversizing = \frac{(Device - Annulus)}{Annulus}\ x\ 100$$



Evolut R Design

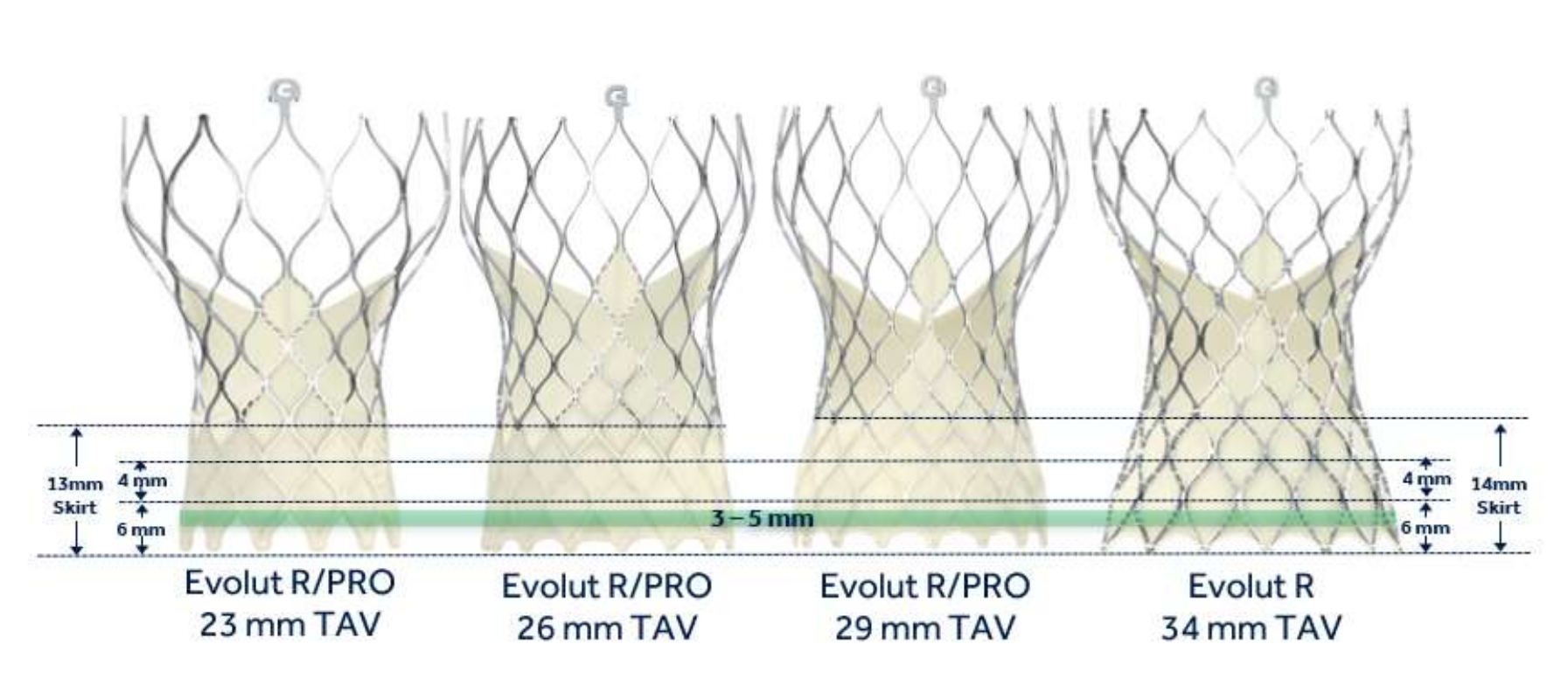
- Minimum oversizing design target acco mplished through:
  - Wider and more cylindrical inflow
  - Indicated sizing range



Evolut TAVR Platform

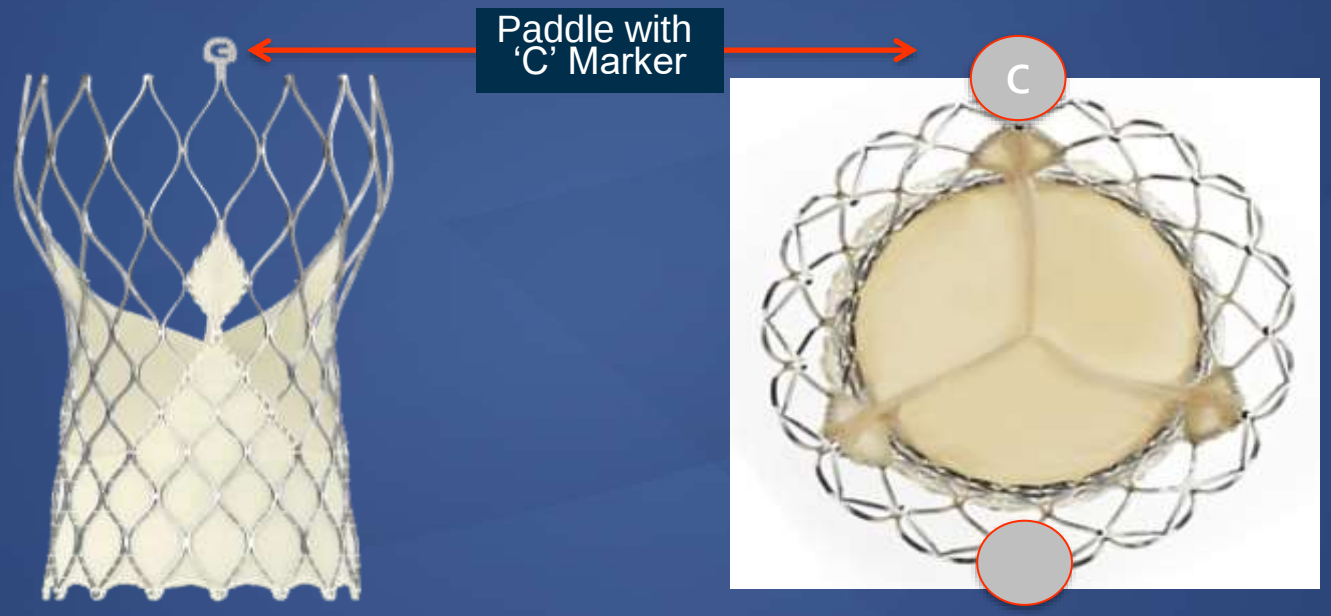
CELL DIMENSIONS & SKIRT HEIGHT

Target implant depth is **3 - 5 mm** for all valve sizes



Note: Measurements provided are approximate based on engineering specifications.

Ease of Use: ‘C’ Paddle Marker

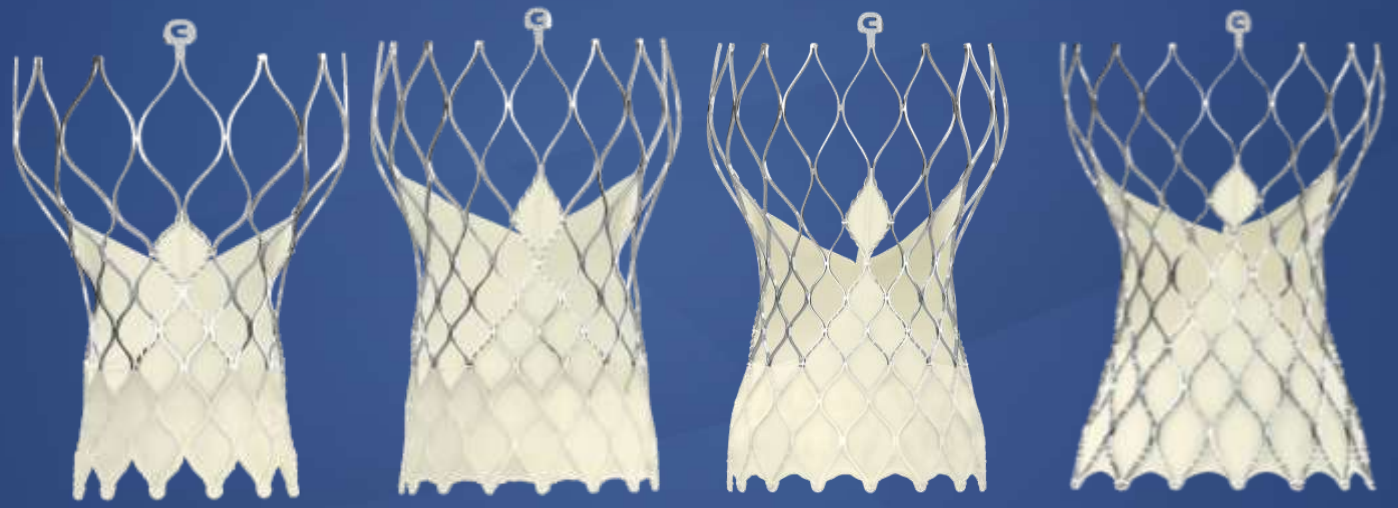


‘C’ marker on one paddle aligns with commissure to help assess post deployment commissure orientation.

Evolut platform

ABILITY TO TREAT BROADEST ANNULUS RANGE

Together, the Evolut PRO and Evolut R Systems treat the widest annulus range of any commercially available TAVR platform*



	Evolut PRO TAV									Evolut R TAV				
	23 mm			26 mm			29 mm			34 mm				
Diameter (mm)	17**	18	19	20	21	22	23	24	25	26	27	28	29	30
Perimeter (mm) †	53.4**	56.5		62.8			72.3			81.7				94.2

* Based on CT measurement

**Measurement for TAV in SAV only. | † Annulus Perimeter = Annulus Diameter x π

Evolut PRO

Intended for Advanced Sealing

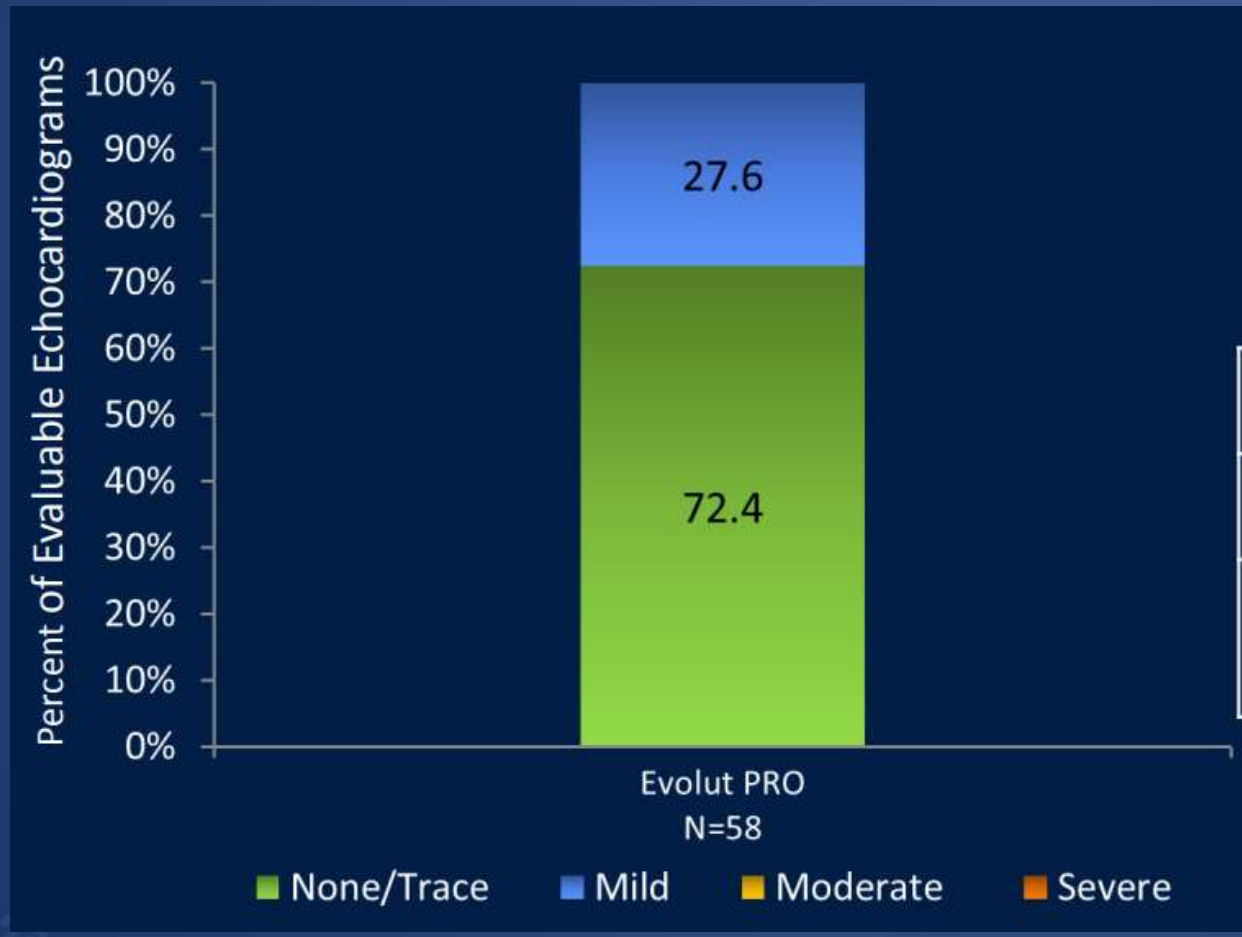
- Conforming frame and consistent radial force provide contact at multiple levels in various annulus shapes
- External tissue wrap increases surface contact area

Proven Platform Performance

- Controlled, accurate deployment with the ability to recapture
- Supra-annular valve function provides unsurpassed hemodynamics
- Lowest delivery profile with integrated InLine Sheath

Evolut PRO

Low rates of PVL while maintain
Low rates of mortality, stroke, and need for pacemaker



30 Day Outcomes

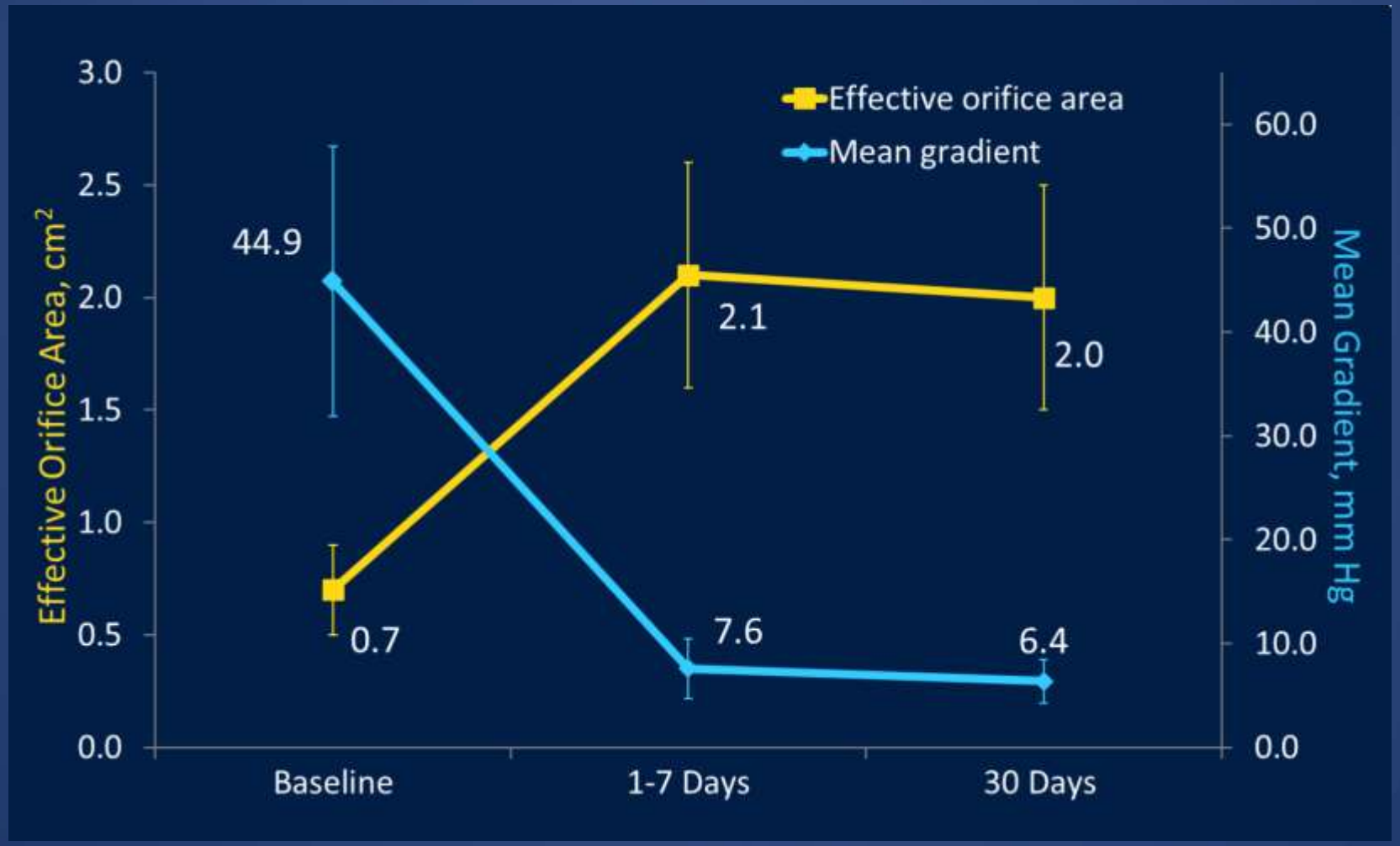
Mortality	**1.7%**
Disabling Stroke	**1.7%**
New Permanent Pacemaker	**10.0%**

Medtronic

Forrest, et al. ACC, 2017

Evolut PRO

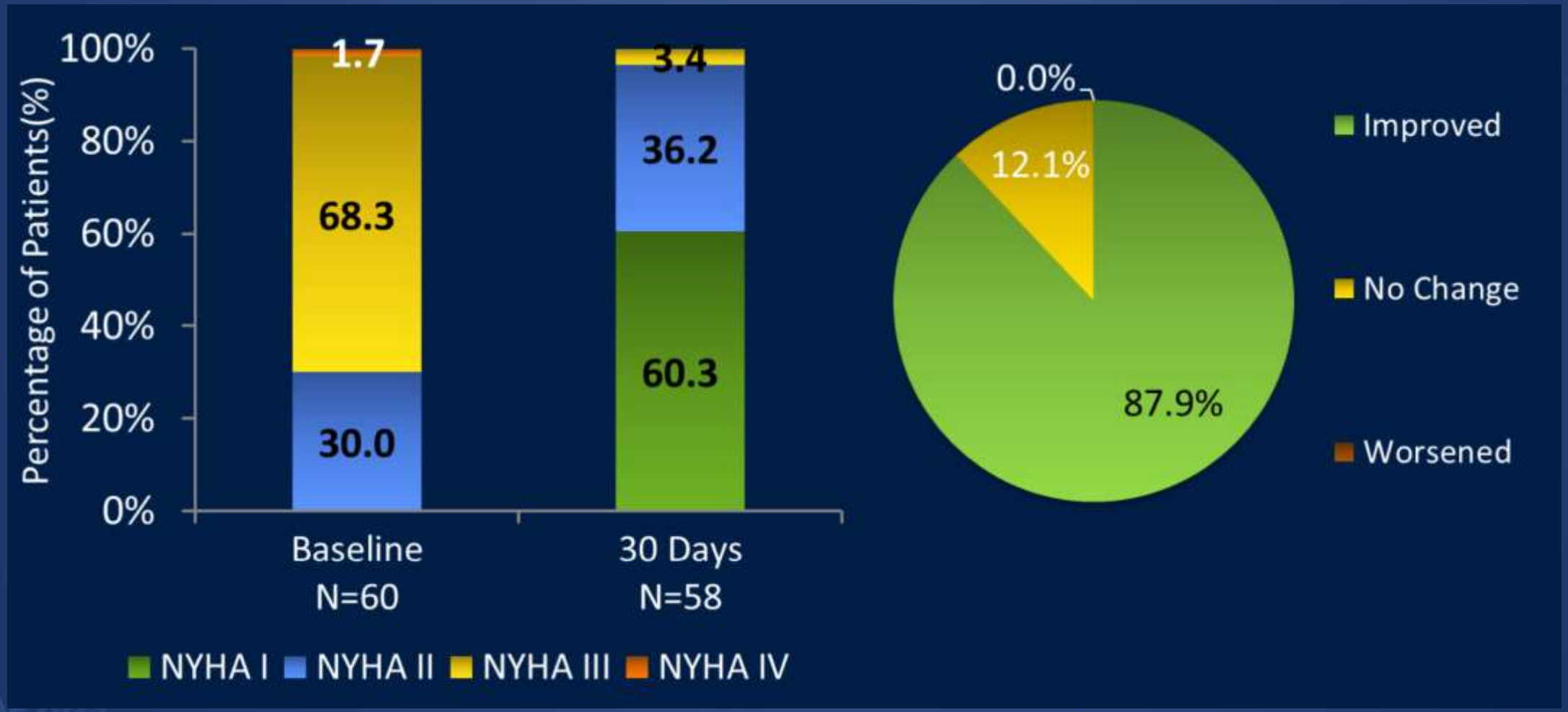
Supra-annular valve function provides single-digit gradients & large effective orifice areas



Forrest, et al. ACC, 2017

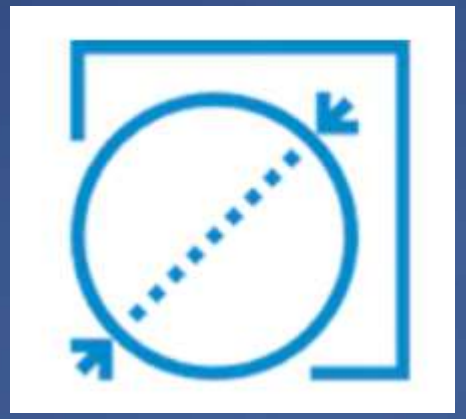
Evolut PRO

87.9% of survivors improved NYHA class at 30days



Forrest, et al. ACC, 2017

Evolut PRO+



Lowest delivery profile

- For access down to 5.0 mm vessels with the 23-29 mm valves

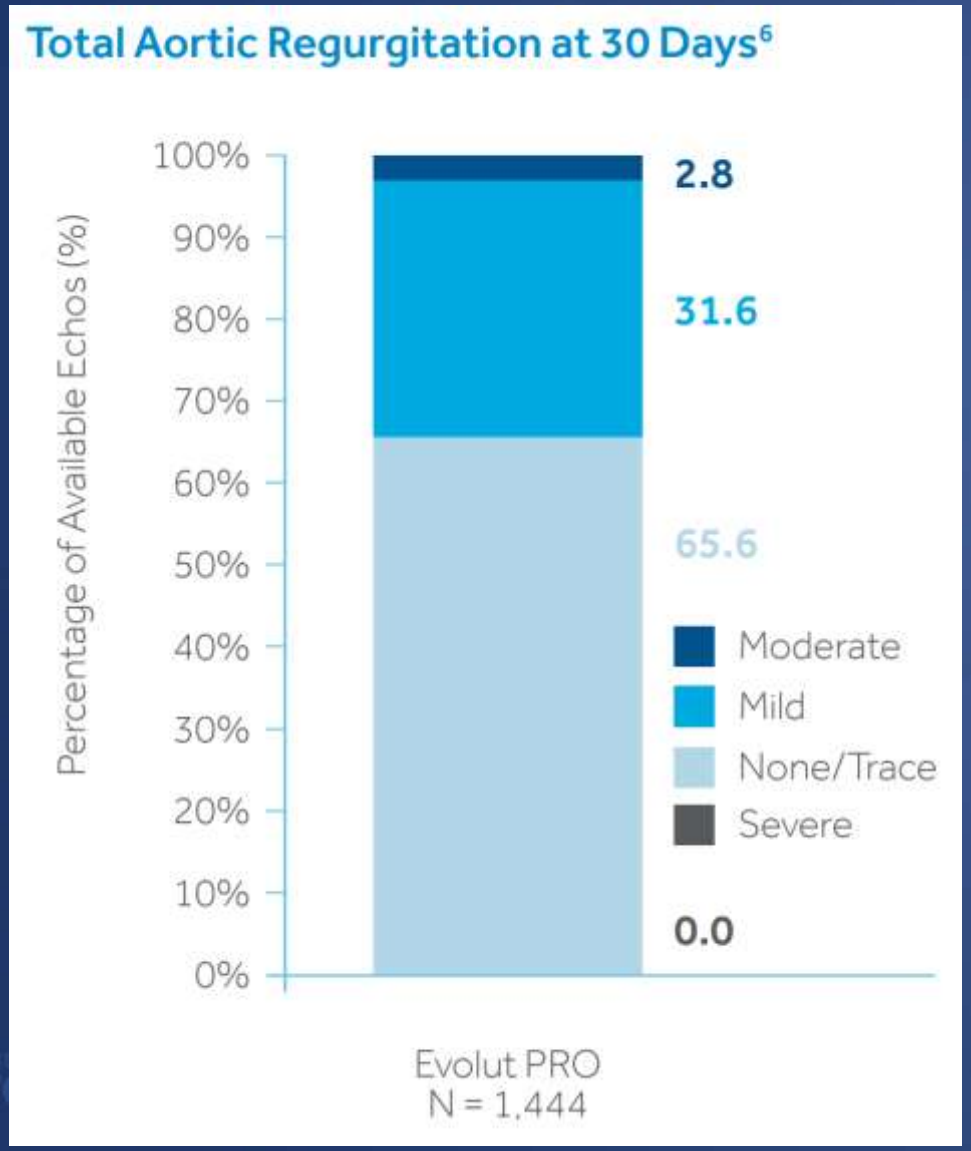
Advanced sealing

- For all valve sized with the addition of the external tissue wrap to the 34 mm valve

Evolut PRO+

Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients. N Engl J Med. May 2, 2019;380(18):1706-1715.

Evolut PRO+



Low Rates of Moderate/Severe PVL

Real-world commercial experience from the STS/ACC TVT Registry™* demonstrates excellent PVL performance.

Forrest JK, Williams MR, Popma JJ, et al. 30-Day Outcomes Following Transcatheter Aortic Valve Replacement With the Evolut PRO Valve in Commercial Use: A Report from the STS/ACC TVT Registry™. Presented at TCT 2018; San Diego, CA.

Medtronic

NOTION TRIAL

NOTION Trial

- First All Comer Trial to Compare TAVR vs. SAVR
- Age ≥70 years
- Self-expanding Bioprosthesis
- Transfemoral or Subclavian Access
- Major Exclusion Criteria
  - Severe CAD
  - Severe other valve disease
  - Prior heart surgery
  - Recent stroke or MI
  - Severe lung or renal disease

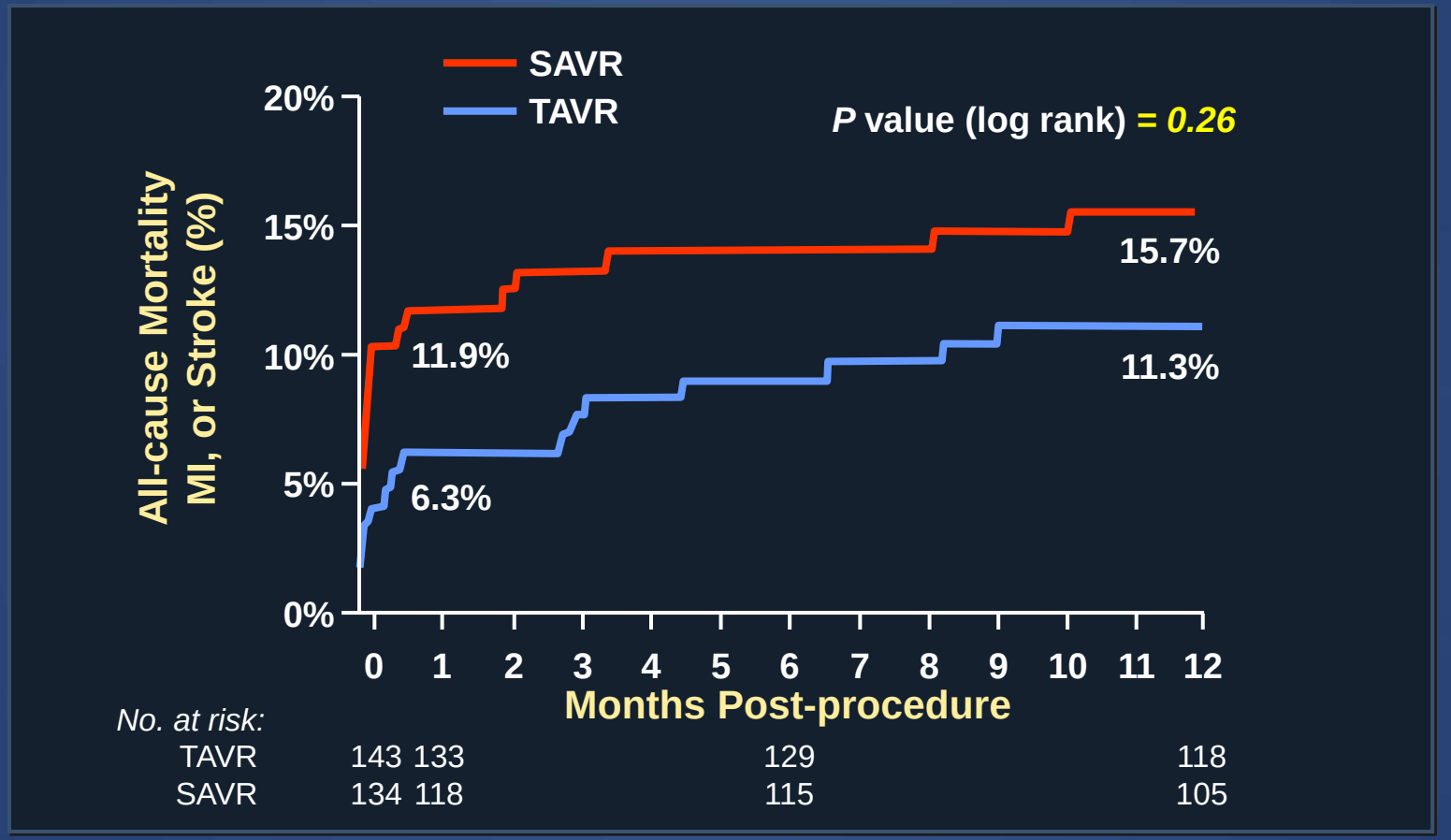
Thyregod HG et al, J Am Coll Cardiol. 2015 May 26;65(20):2184-94
Lars Søndergaard et al, Circ Cardiovasc Interv. 2016;9:e003665

NOTION Trial: Baseline Characteristics

Characteristic, % or mean ± SD	TAVR n=145	SAVR n=135	*P* value
Age (yrs)	79.2 ± 4.9	79.0 ± 4.7	0.71
Male	53.8	52.6	0.84
Society of Thoracic Surgeons (STS) Score	2.9 ± 1.6	3.1 ± 1.7	0.30
STS Score < 4%	83.4	80.0	0.46
Logistic EuroSCORE I	8.4 ± 4.0	8.9 ± 5.5	0.38
NYHA class III or IV	48.6	45.5	0.61

Thyregod HG et al, J Am Coll Cardiol. 2015 May 26;65(20):2184-94
Lars Søndergaard et al, Circ Cardiovasc Interv. 2016;9:e003665

NOTION Trial: Death, Stroke, or MI



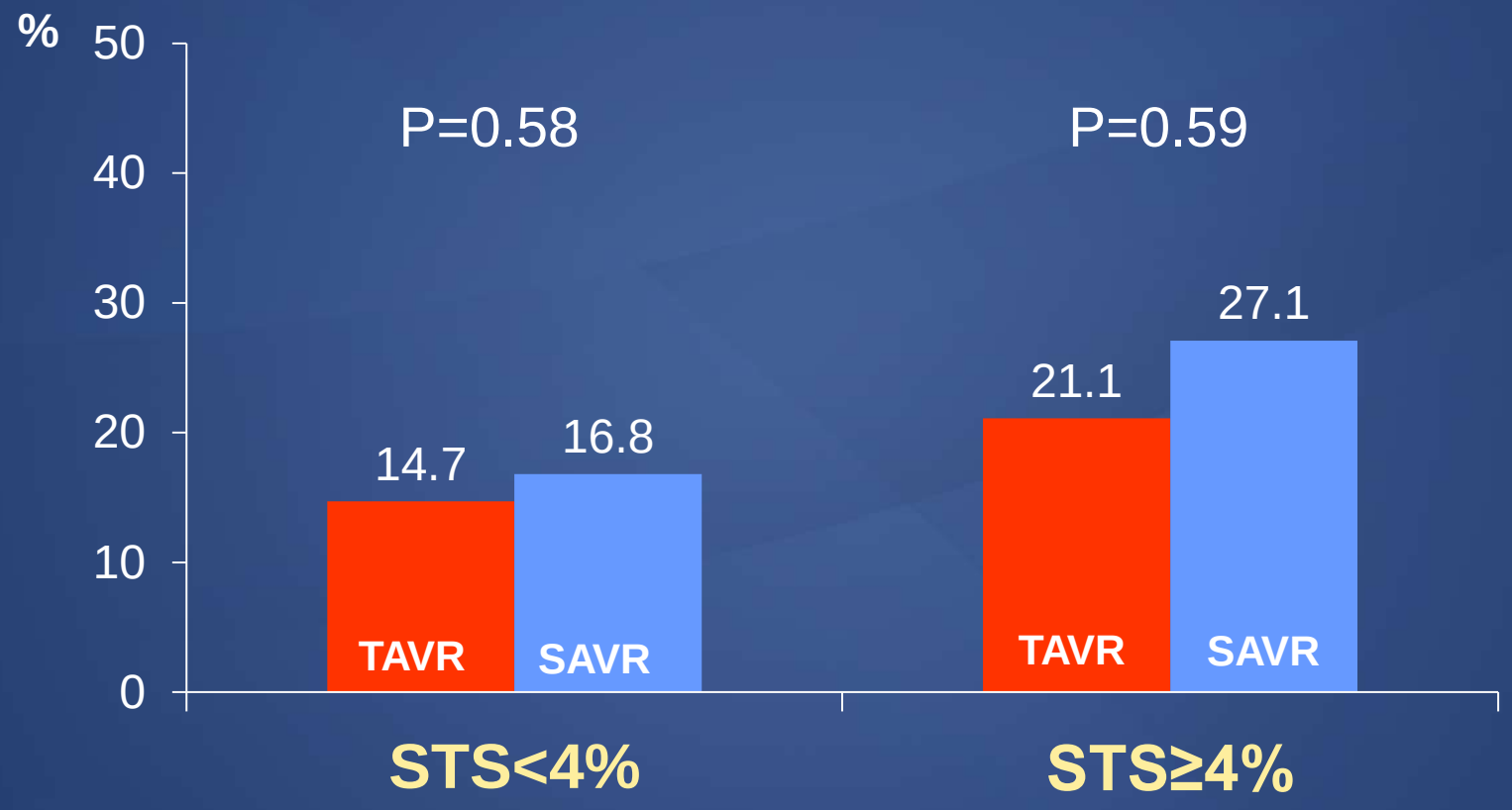
Thyregod HG et al, J Am Coll Cardiol. 2015 May 26;65(20):2184-94
Lars Søndergaard et al, Circ Cardiovasc Interv. 2016;9:e003665

NOTION Trial @ 2 Years

Events (%)	No of Pts With Events (%)		
	TAVR	SAVR	P Value
All-Cause Death	11 (8.0)	13 (9.8)	0.54
Cardiovascular Death	9 (6.5)	12 (9.1)	0.40
Neurologic Events	13 (9.7)	10 (7.8)	0.67
Stroke	5 (3.6)	7 (5.4)	0.46
TIA	8 (6.0)	4 (3.3)	0.30
Myocardial Infarction	7 (5.1)	8 (6.0)	0.69
New-Onset of Worsening A.fib	32 (22.7)	80 (60.2)	<0.001
PPM Implantation	55 (41.3)	5 (4.2)	<0.001
PVL ≥ Moderate	19 (15.4)	1 (0.9)	<0.001

Thyregod HG et al, J Am Coll Cardiol. 2015 May 26;65(20):2184-94
Lars Søndergaard et al, Circ Cardiovasc Interv. 2016;9:e003665

NOTION Trial : Death, MI, or Stroke @ 2 Years



Thyregod HG et al, J Am Coll Cardiol. 2015 May 26;65(20):2184-94
Lars Søndergaard et al, Circ Cardiovasc Interv. 2016;9:e003665

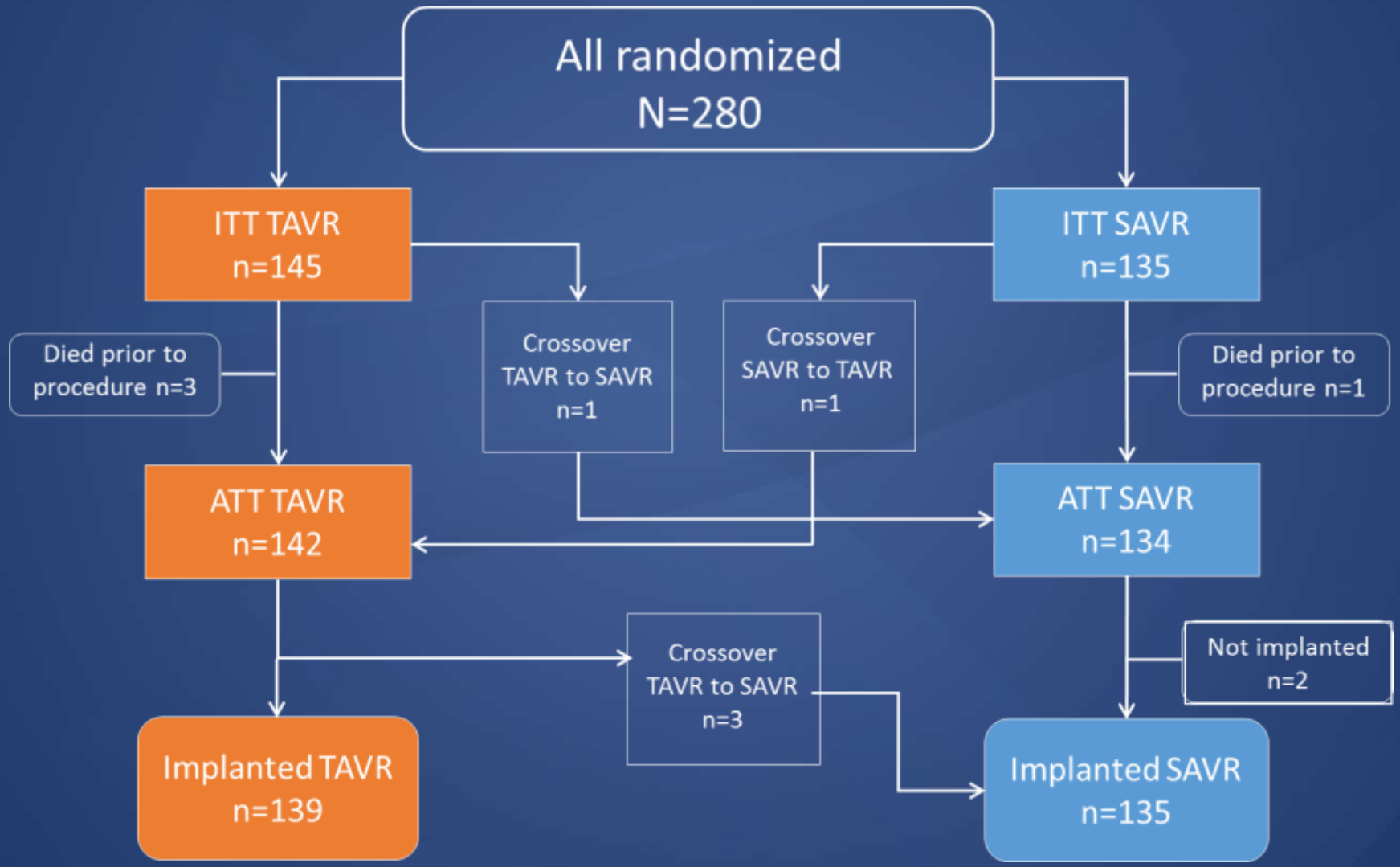
NOTION Trial

Long-Term (> 5years) Outcomes of TAVR vs SAVR In Low-Risk Patients

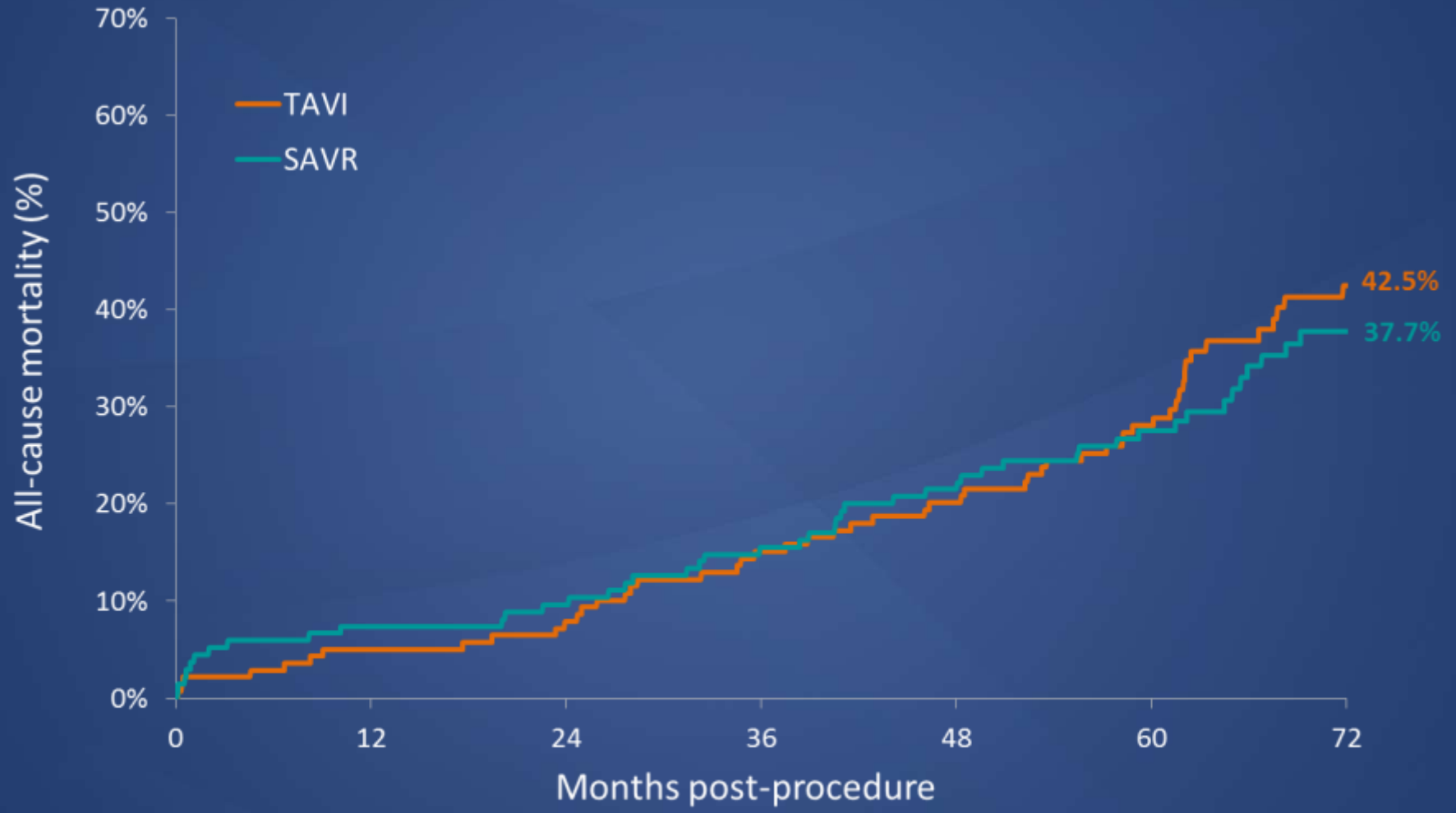
Lars Søndergaard et al, J Am Coll Cardiol. 2019;73:546–53

NOTION Trial

Trial Flow



NOTION Trial: 6 year Results
All-cause mortality



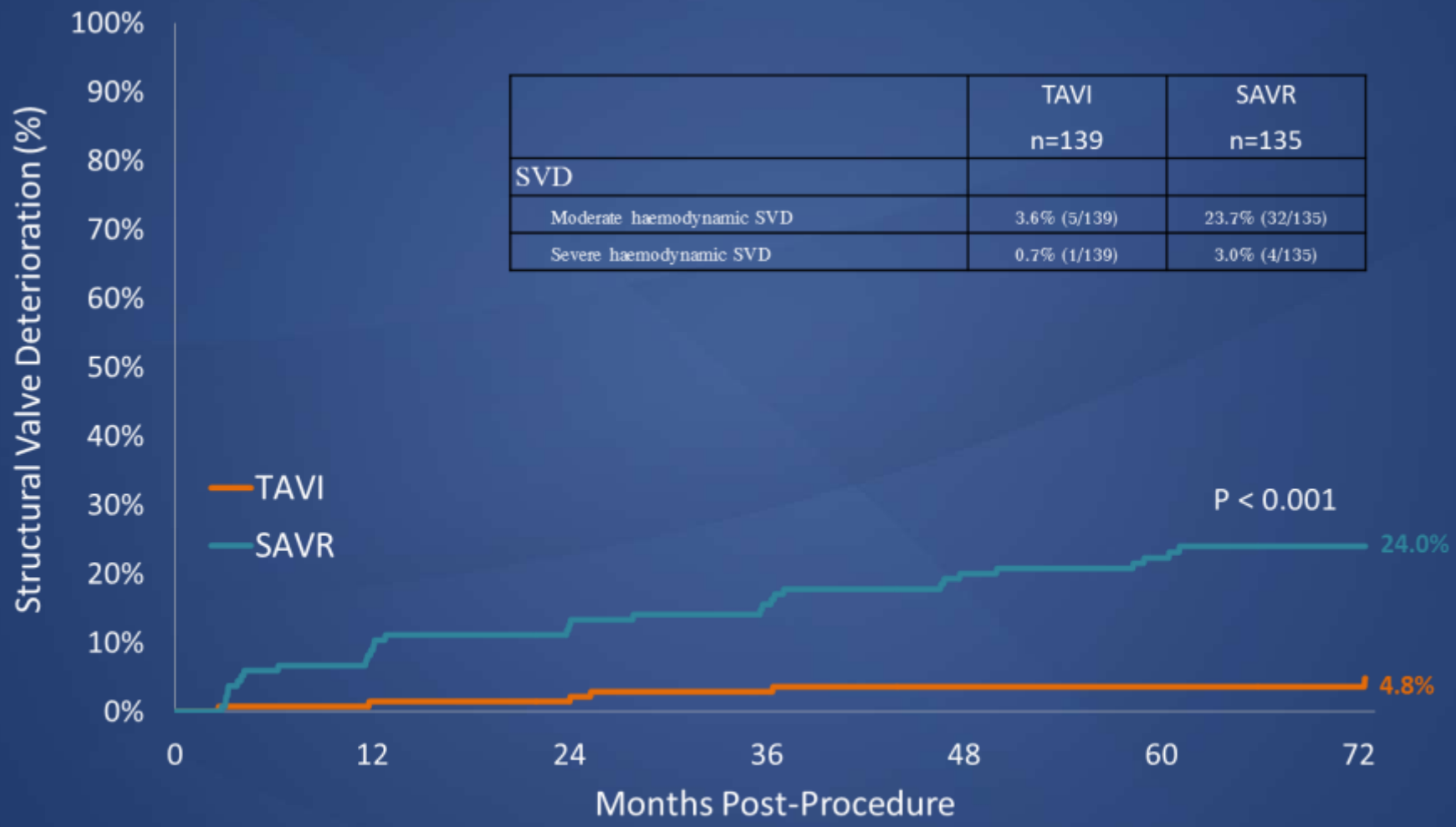
Number at risk:

139 136	132	128	118	111	88	46
135 130	125	122	114	104	88	48

NOTION Trial: 6 year Results
Aortic valve performance

NOTION Trial: 6 year Results
Structural valve deterioration

	TAVI n=139	SAVR n=135
SVD		
Moderate haemodynamic SVD	3.6% (5/139)	23.7% (32/135)
Severe haemodynamic SVD	0.7% (1/139)	3.0% (4/135)



Number at risk:

139	134	130	125	114	106	84	44
135	119	113	104	95	81	70	32

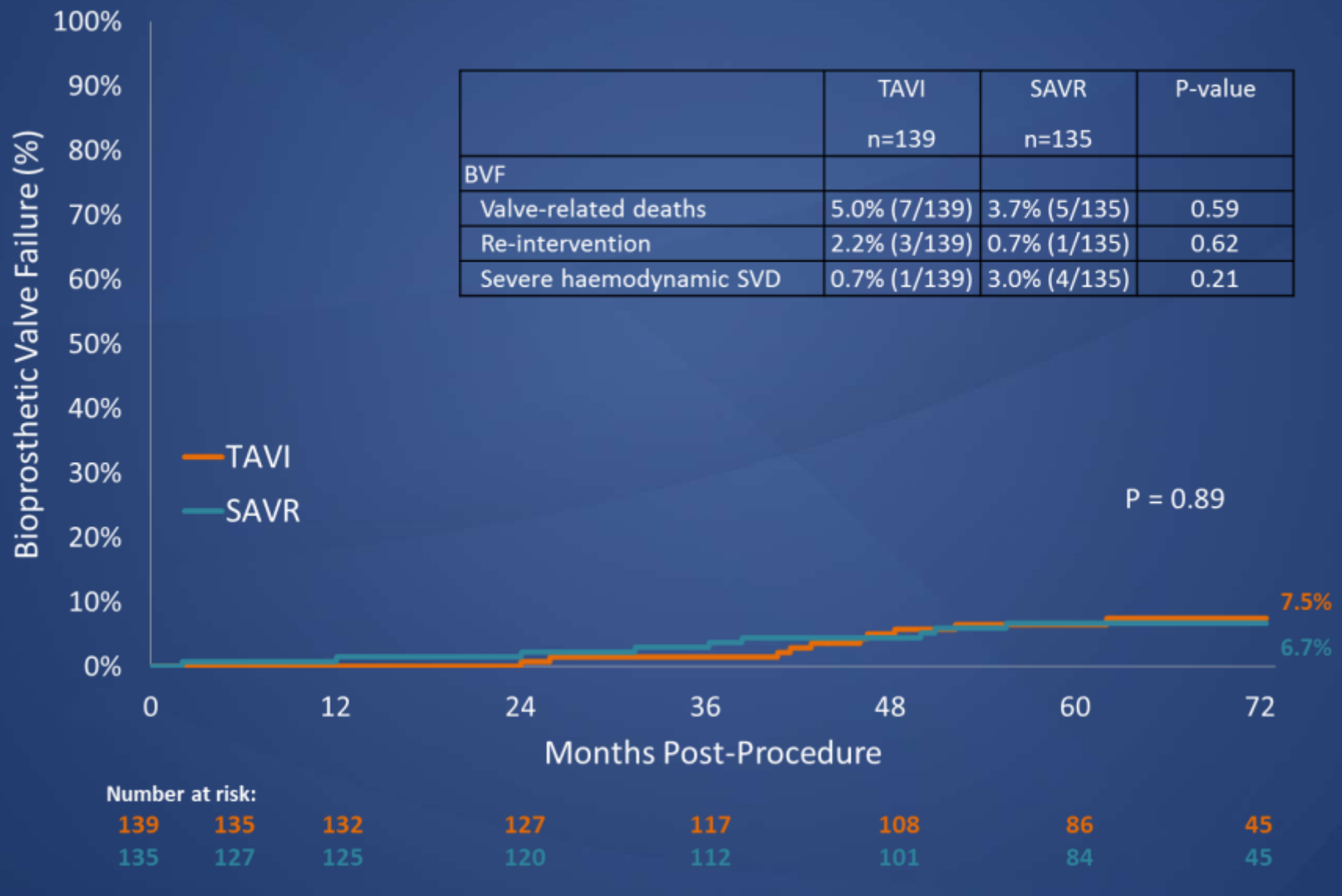
NOTION Trial
Durability analysis methods

- SVD
  - Moderate or severe haemodynamic SVD
    - Mean gradient ≥20 mmHg *or*
    - Mean gradient ≥10 mmHg change from baseline *or*
    - Moderate/severe intra-prosthetic aortic regurgitation (AR) (new or worsening from baseline)
- NSVD
  - Moderate/severe patient-prosthesis mismatch (PPM) at 3 months *or*
  - Moderate/severe paravalvular regurgitation (PVL)

Capodanno et al. Eur Heart J. 2017; 38:3382-90

NOTION Trial: 6 year Results
Bioprosthetic valve failure

	TAVI n=139	SAVR n=135	P-value
BVF			
Valve-related deaths	5.0% (7/139)	3.7% (5/135)	0.59
Re-intervention	2.2% (3/139)	0.7% (1/135)	0.62
Severe haemodynamic SVD	0.7% (1/139)	3.0% (4/135)	0.21

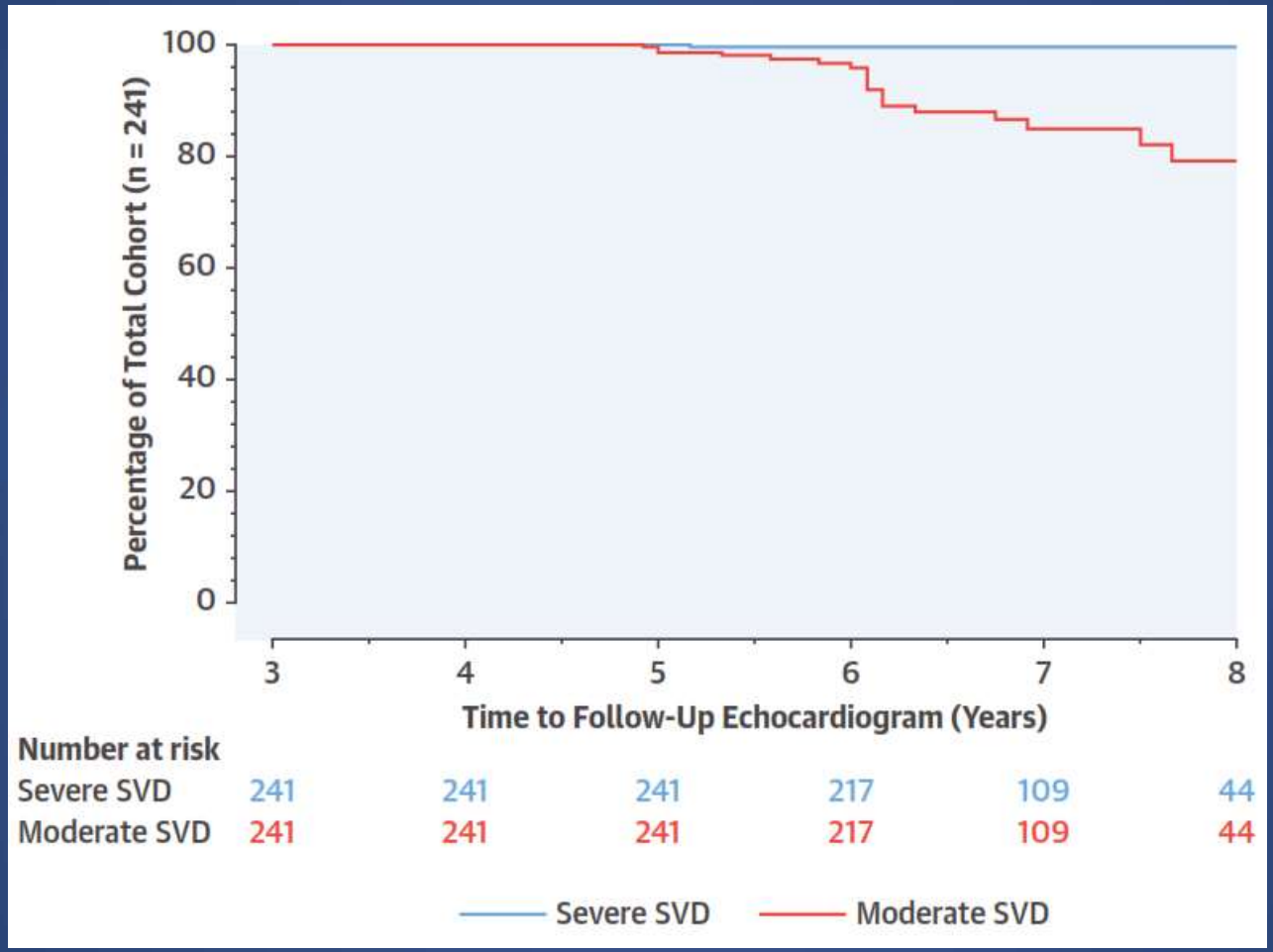


The U.K. TAVI registry

Long-Term Durability of Transcatheter Aortic Valve Prostheses

Daniel J. Blackman et al, J Am Coll Cardiol. 2019;73:537–45

UK TAVI Registry
Freedom From Structural Valve Deterioration Over Time



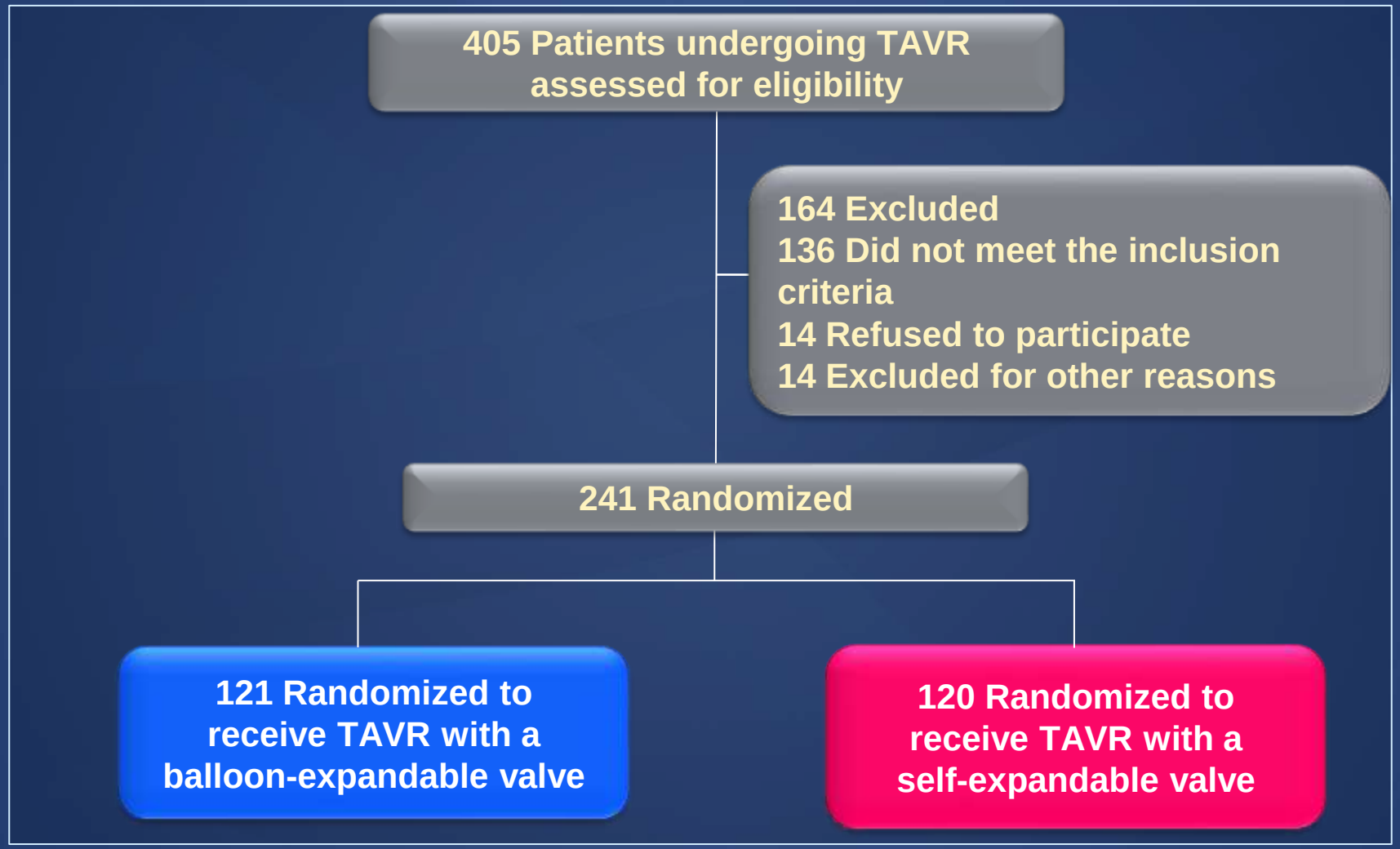
Severe SVD 1 case (0.4%) - 5.3 years after implantation (new severe AR)

Moderate SVD 21 cases (8.7%) - mean 6.1 years post-TAVR; range 4.9 to 8.6 years

CoreValve vs. Edwards SAPIEN XT

CHOICE TRIAL

CHOICE trial : Study Design



Abdel-Wahab M, Mehilli J, Frerker C et al. JAMA 2014 Mar 30. [Epub ahead of print]

CHOICE Trial : Procedural Outcome

	Balloon-expandable Valve N=121	Self-expandable Valve N=120	P Value
Immediate procedural mortality, %	0	0	
Final aortic regurgitation			
Angiography, %			
Moderate	3.3	14.1	< 0.001
Severe	0.8	4.2	
Echocardiography, %			
Moderate	0.8	5.8	< 0.005
Severe	0.8	0	
Device success (primary endpoint)	95.9	77.5	< 0.001

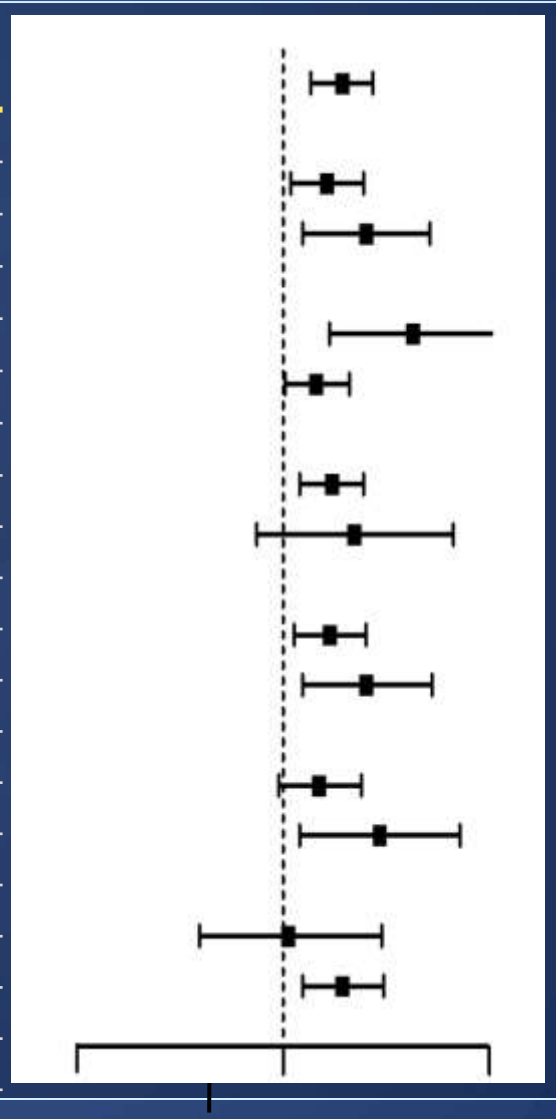
Adams DH, Popma JJ, Reardon MJ, et al. New Engl J Med 2014; Mar 29, [Epub ahead of print]

CHOICE Trial : 30-Day Clinical Outcome

Variables	Balloon-expandable Valve N=121	Self-expandable Valve N=120	P Value
Death, %			
Any cause	4.1	5.1	0.77
Cardiovascular causes	4.1	4.3	0.99
Stroke	5.8	2.6	0.33
Life threatening bleeding	8.3	12.0	0.35
Major bleeding	19.0	14.5	0.36
Vascular complications	14.0	12.8	0.78
Acute kidney injury	4.1	1.7	0.13
Rehospitalization for heart failure	0.0	4.3	0.02
NYHA class improvement	94.3	86.7	0.06
New permanent pacemaker	17.3	37.6	0.001

CHOICE trial
Subgroup Analyses for Device Success

Subgroup	Balloon-expandable Valve	Self-expandable Valve	Relative Risk (95% CI)
Overall	95.9	77.5	1.24 (1.12-1.37)
Age, y			
≥80	96.5	81.6	1.18 (1.05-1.33)
<80	94.4	70.4	1.34 (1.09-1.65)
Sex			
Men	96.1	61.8	1.56 (1.19-2.04)
Women	95.6	83.7	1.14 (1.03-1.27)
LV ejection fraction			
>35	96.0	80.0	1.20 (1.08-1.33)
≤35	94.7	73.3	1.29 (0.94-1.78)
Mitral regurgitation			
None/mild	96.0	80.8	1.19 (1.06-1.34)
Moderate/severe	95.5	71.1	1.34 (1.09-1.66)
CT annulus diameter, mm			
<25	93.3	80.9	1.14 (1.01-1.32)
≥25	97.1	69.2	1.40 (1.08-1.82)
Aortic leaflet calcification			
None/mild	88.9	85.0	1.04 (0.78-1.41)
Moderate/severe	95.3	76.7	1.24 (1.09-1.42)



CHOICE Trial

	Balloon-expandable Valve N=121	Self-expandable Valve N=120	P Value
Device success (primary endpoint)	95.9	77.5	< 0.001
30-day clinical outcomes			
Death, %			
Any cause	4.1	5.1	0.77
Cardiovascular causes	4.1	4.3	0.99
Stroke	5.8	2.6	0.33
Life threatening bleeding	8.3	12.0	0.35
Vascular complications	14.0	12.8	0.78
Rehospitalization for heart failure	0.0	4.3	0.02
NYHA class improvement	94.3	86.7	0.06
New permanent pacemaker	17.3	37.6	0.001

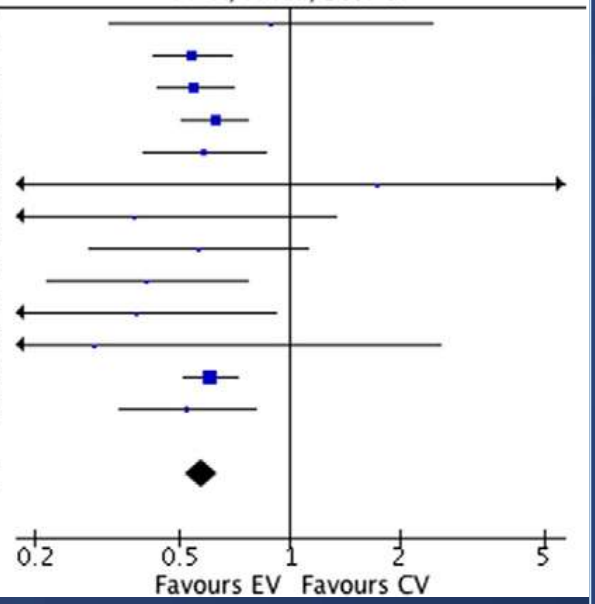
CoreValve vs. SAPIEN XT

Meta-analysis

Study or Subgroup	EV Events	EV Total	CV Events	CV Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chieffo 2013	6	340	9	453	0.8%	0.89 [0.32, 2.47]
DiMaro 2012	98	1472	130	1050	16.4%	0.54 [0.42, 0.69]
Dworakowski 2014	96	1287	157	1153	17.9%	0.55 [0.43, 0.70]
Gilard 2012	174	2107	138	1043	19.9%	0.62 [0.51, 0.77]
Hayashida 2012	80	347	21	53	3.9%	0.58 [0.40, 0.85]
Hernandez-Antolin 2011	1	37	0	21	0.1%	1.74 [0.07, 40.83]
Kasel 2014	3	50	8	50	0.9%	0.38 [0.11, 1.33]
Nombela-Franco 2013	9	41	16	41	1.7%	0.56 [0.28, 1.12]
Spargias 2013	10	59	28	67	2.8%	0.41 [0.22, 0.76]
Spethmann 2012	5	48	27	98	1.9%	0.38 [0.16, 0.92]
Tchetche 2010	1	24	3	21	0.3%	0.29 [0.03, 2.60]
Van Belle 2014	243	1872	193	897	28.2%	0.60 [0.51, 0.72]
Wantabe 2013	26	170	44	150	5.1%	0.52 [0.34, 0.80]
Total (95% CI)		**7854**		**5097**	**100.0%**	**0.57 [0.52, 0.63]**
Total events	752		774			

Heterogeneity: $Chi^2 = 5.53$, $df = 12$ ($P = 0.94$); $I^2 = 0\%$

Test for overall effect: $Z = 11.42$ ($P < 0.00001$)



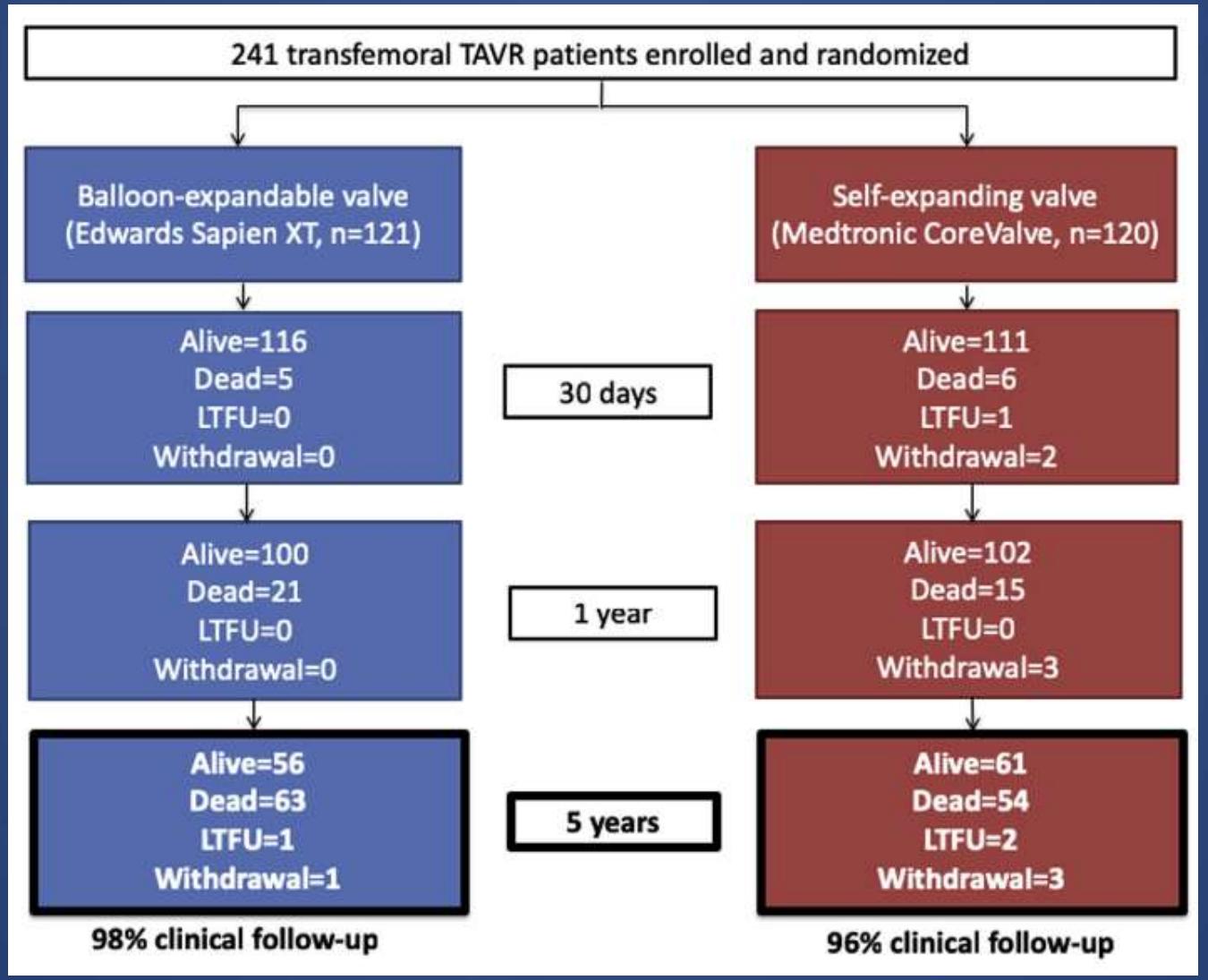
Conclusion: CoreValve is associated with higher incidence of post-TAVR moderate to severe paravalvular AR.

Bhatheja et al., Cardiovasc Revasc Med 2016

CoreValve vs. Edwards SAPIEN XT

CHOICE TRIAL
5-Year Outcomes

CHOICE Trial
5-Year Outcomes



Abdel-Wahab, M. et al. J Am Coll Cardiol Intv. 2020;13(9):1071–82.

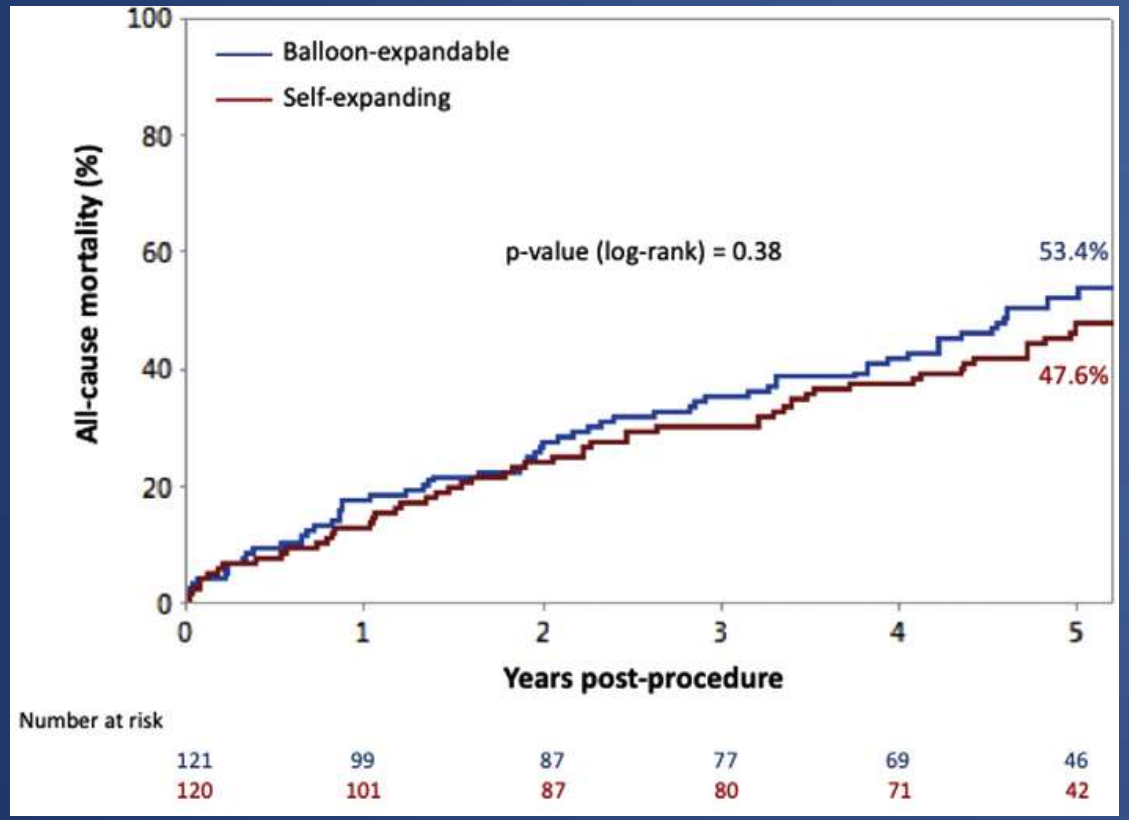
CHOICE Trial
5-Year Outcomes

	Balloon-Expandable Valve (n = 121)	Self-Expanding Valve (n = 120)	p Value
Death			
From any cause	63 (53.4)	54 (47.6)	0.38
From cardiovascular causes	37 (31.6)	25 (21.5)	0.12
Stroke	21 (17.5)	19 (16.5)	0.73
Repeat hospitalization for heart failure	30 (28.9)	26 (22.5)	0.75
Myocardial infarction	2 (1.6)	7 (6.1)	0.08
Bleeding			
Life threatening	21 (17.3)	18 (16.2)	0.77
Major	28 (26.3)	20 (22.0)	0.26
Minor	17 (14.3)	12 (10.4)	0.37
Vascular complications			
Major	14 (11.6)	14 (12.1)	0.89
Minor	5 (4.2)	3 (2.6)	0.51
New pacemaker*	28 (25.4)	40 (40.4)	0.01

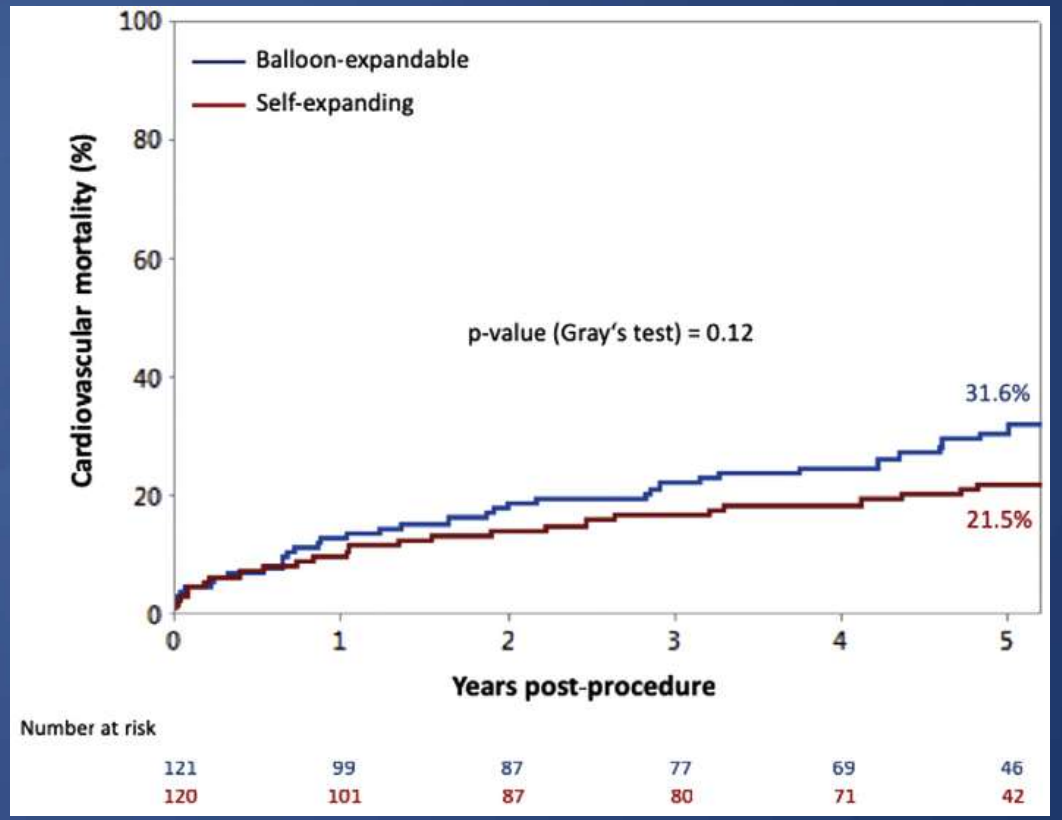
Abdel-Wahab, M. et al. J Am Coll Cardiol Intv. 2020;13(9):1071–82.

CHOICE Trial
5-Year Outcomes

All-cause mortality



Cardiovascular mortality



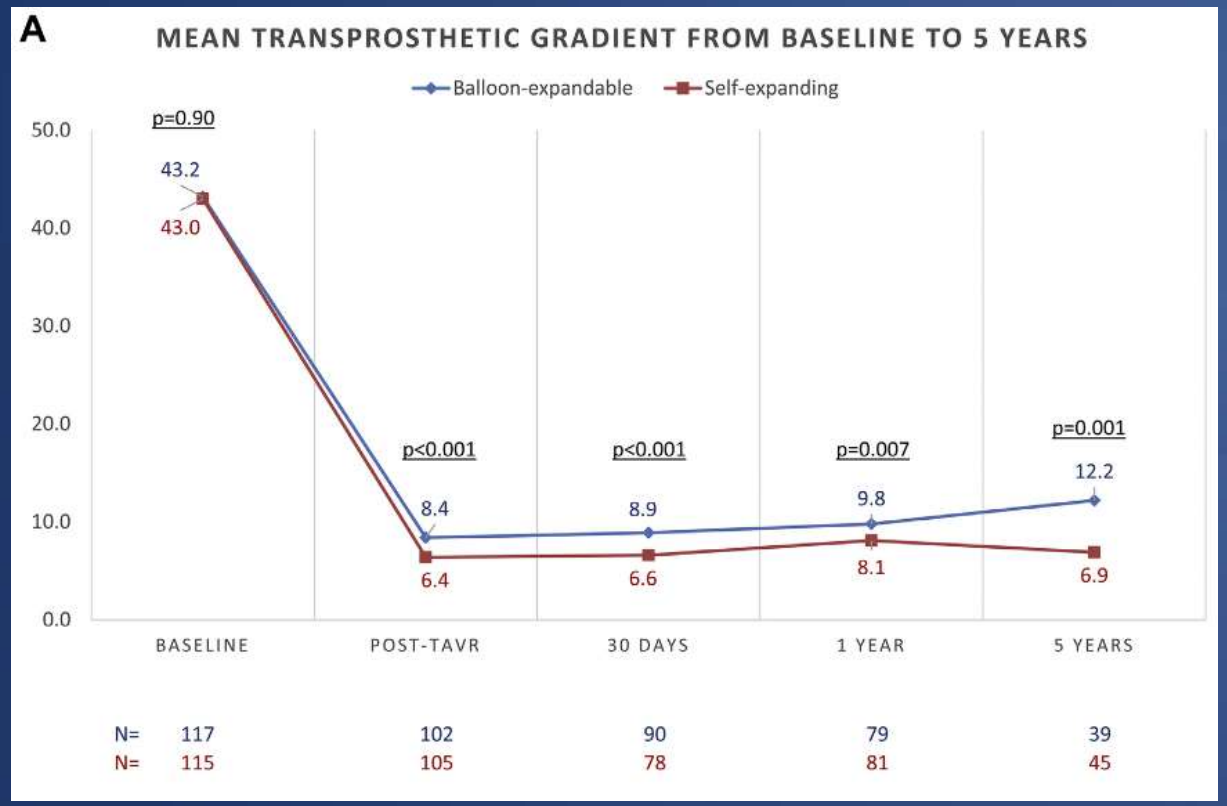
Abdel-Wahab, M. et al. J Am Coll Cardiol Intv. 2020;13(9):1071–82.

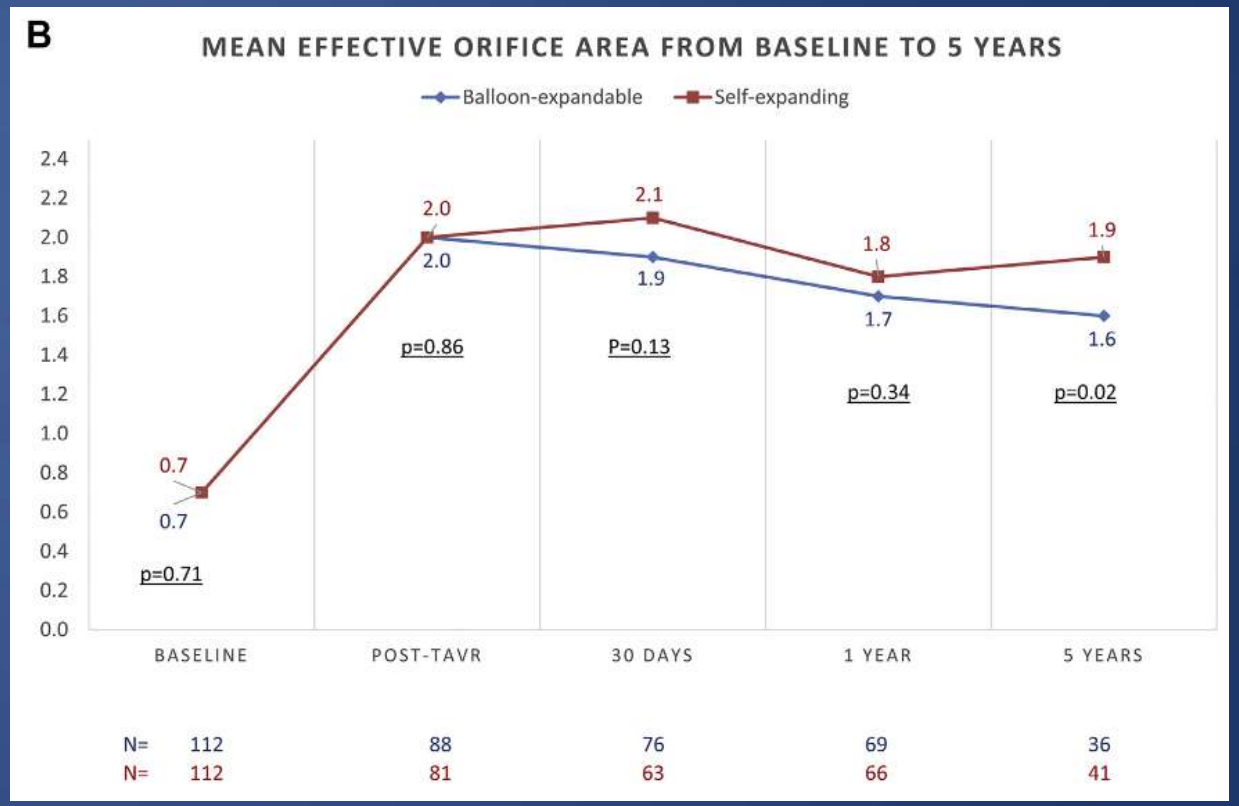
CHOICE Trial
5-Year Outcomes
Echocardiographic F/U at 5 years

	Balloon-Expandable Valve (n = 36)	Self-Expanding Valve (n = 41)	p Value
Effective orifice area, cm^2	1.6 ± 0.5	1.9 ± 0.5	0.02
Number of patients	39	45	
Mean gradient, mm Hg	12.2 ± 8.7	6.9 ± 2.7	0.001
Number of patients	47	52	
Transvalvular aortic regurgitation			0.62
None/trace	46 (97.9)	49 (94.2)	
Mild	1 (2.1)	3 (5.8)	
Moderate	0 (0.0)	0 (0.0)	
Severe	0 (0.0)	0 (0.0)	
Number of patients	47	52	
Paravalvular aortic regurgitation			0.69
None/trace	28 (59.6)	28 (53.8)	
Mild	19 (40.4)	24 (46.2)	
Moderate	0 (0.0)	0 (0.0)	
Severe	0 (0.0)	0 (0.0)	
Number of patients	47	52	
Total aortic regurgitation			0.42
None/trace	27 (57.4)	25 (48.1)	
Mild	20 (42.6)	27 (51.9)	
Moderate	0 (0.0)	0 (0.0)	
Severe	0 (0.0)	0 (0.0)	
Left ventricular ejection fraction, %	54.4 ± 10.2	57.2 ± 8.4	0.15
Left ventricular end-systolic dimension, mm	34.4 ± 12.0	29.1 ± 6.7	0.02
Left ventricular end-diastolic dimension, mm	45.5 ± 7.7	41.7 ± 6.8	0.02
Systolic pulmonary artery pressure, mm Hg	30.9 ± 12.0	29.0 ± 12.7	0.49
Moderate/severe mitral regurgitation	15/47 (31.9)	9/48 (18.7)	0.13
Moderate/severe tricuspid regurgitation	10/45 (22.2)	13/47 (27.6)	0.54

Abdel-Wahab, M. et al. J Am Coll Cardiol Intv. 2020;13(9):1071–82.

CHOICE Trial
5-Year Outcomes
Forward-Flow Hemodynamics From Baseline to 5 Years



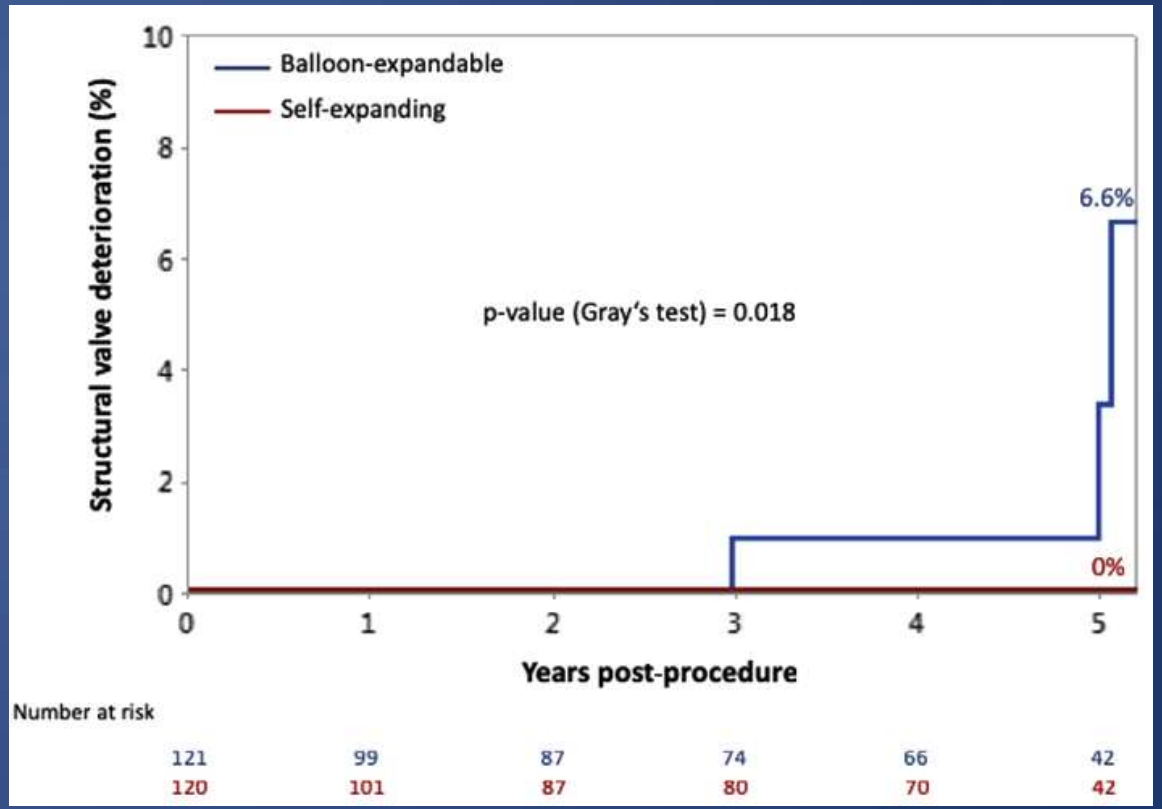


Abdel-Wahab, M. et al. J Am Coll Cardiol Intv. 2020;13(9):1071–82.

CHOICE Trial
5-Year Outcomes
Bioprosthetic valve dysfunction through 5 Years

	Balloon-Expandable Valve (n = 121)	Self-Expanding Valve (n = 120)	p Value
Bioprosthetic valve dysfunction	28 (22.5)	26 (20.9)	0.91
Components			
SVD	6 (6.6)	0 (0.0)	0.018
Moderate SVD	4 (5.6)	0 (0.0)	0.047
Severe SVD	2 (0.9)	0 (0.0)	0.20
NSVD	17 (17.8)	23 (26.7)	0.20
Moderate/severe PPM	14 (15.9)	13 (16.0)	1.0
Moderate/severe PVL	3 (2.5)	10 (8.5)	0.08
Valve thrombosis	6 (7.3)	1 (0.8)	0.06
Endocarditis	2 (1.6)	4 (3.4)	0.39

SVD = structural valve deterioration
NSVD = nonstructural valve deterioration
PPM = patient-prosthesis mismatch
PVL = paravalvular leak



Structural Valve Deterioration in the CHOICE trial

Abdel-Wahab, M. et al. J Am Coll Cardiol Intv. 2020;13(9):1071–82.

Direct TAVR vs. Pre-balloon TAVR

Case matched Analysis

Variables	Direct (n=102)	Pre-BAV (n=102)	P-value
Self-expandable	32 (31.7%)	32 (31.7%)	>0.999
Balloon-Ex	70 (68.6%)	70 (68.6%)	>0.999
Prosthesis size (mm)			
23	33 (32.4%)	33 (32.4%)	>0.999
26	48 (47.1%)	48 (47.1%)	>0.999
29	21 (20.6%)	21 (20.6%)	>0.999
Device success	93 (91.2%)	92 (90.2%)	0.810
Post-dilatation	18 (17.6%)	25 (24.5%)	0.356
Need for a Second valve	4 (3.9%)	5 (4.9%)	0.568
Contrast (ml)	137.2± 66.9	167.5 83	0.003
Procedure time (min)	94.7 ± 35.9	135.1± 51.1	<0.001

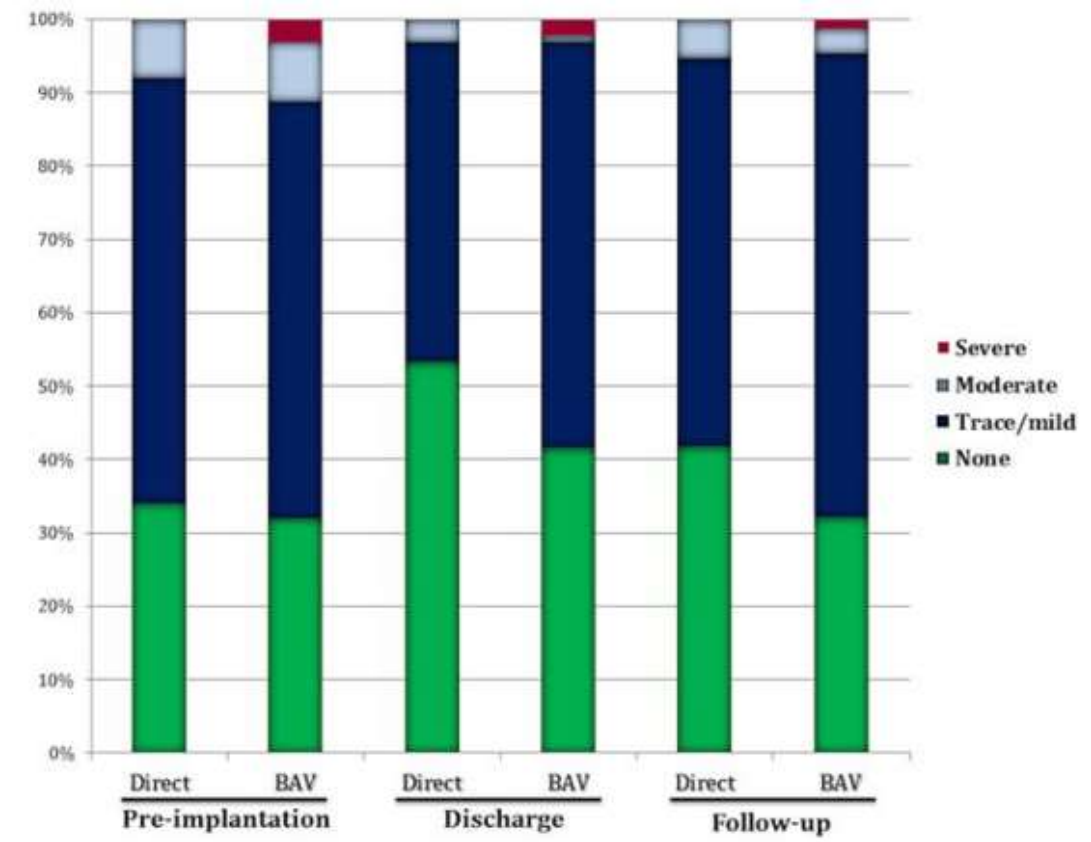
Ferrera C, et al. Cath Cardiovasc Int 2016 online publication

Post TAVR outcomes

Variables	Direct (n=102)	Pre-BAV (n=102)	P-value
Valvular regurgitation			
Moderate	8 (7.8%)	9 (8.9%)	0.767
Severe	0 (0%)	3 (2.9%)	0.557
Paravalvular regurgitation			
Moderate	3 (3.0%)	1 (1.0%)	0.106
Severe	0 (0%)	2 (2.0%)	0.106
Valve area (cm^2)	2.1±0.48	1.84±0.47	0.106
Peak gradient (mmHg)	15.9±7.7	15.2±5.6	0.588
Mean gradient (mmHg)	8.08±4.5	8.28±3.7	0.454

Ferrera C, et al. Cath Cardiovasc Int 2016 online publication

Paravalvular regurgitation



A trend toward a higher proportion of none paravalvular leakage was observed in the direct implantation group (P=0.09).

Ferrera C, et al. Cath Cardiovasc Int 2016 online publication

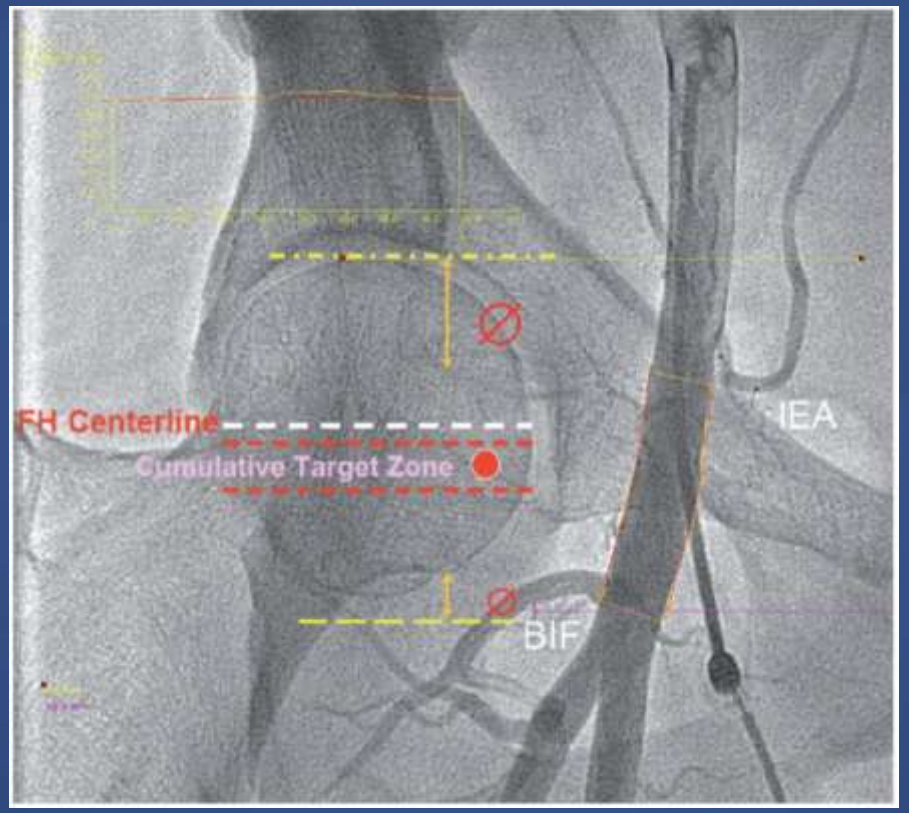
Clinical outcomes at 12 months

Variables	Direct (n=102)	Pre-BAV (n=102)	P-value
Major Vascular Complication	9 (10.1%)	15 (14.9%)	0.326
Need for permanent PM	15 (15.0%)	20 (19.6%)	0.339
Stroke	3 (2.9%)	2 (2.0%)	0.571
Acute Kidney Injury (Grade 2 or 3)	0 (0%)	12 (12.2%)	0.001
In-hospital stay (days)	9.9	8.8	0.403
Death (30-day)	5 (4.9%)	10 (9.8%)	0.177
Death (12 months)	9 (14.0%)	20 (23.8%)	0.771

Ferrera C, et al. Cath Cardiovasc Int 2016 online publication

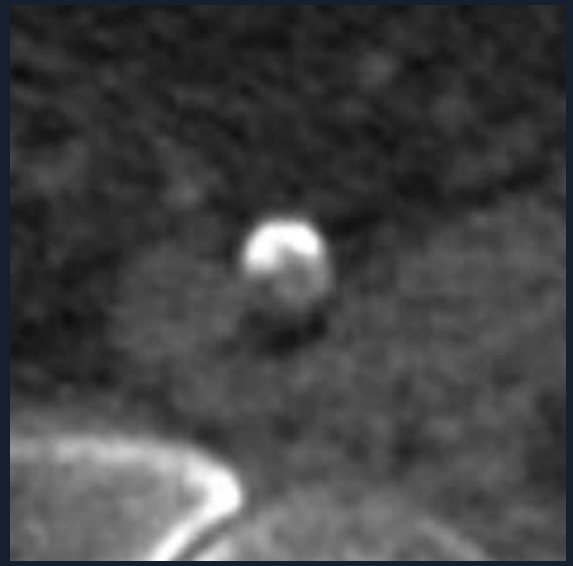
TAVR
Vascular Closure Device

Puncture Site

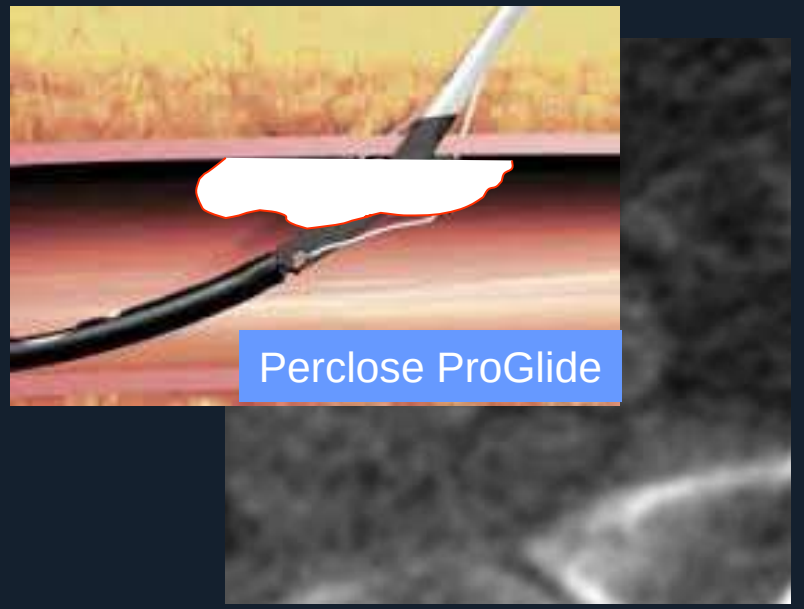


Puncture Site

If there is anteriorly located calcium at puncture site, surgical cut-down would be safer than using percutaneous approach



Anteriorly Located Calcium



Posteriorly Located Calcium

Proglide® Abbott Vascular Devices

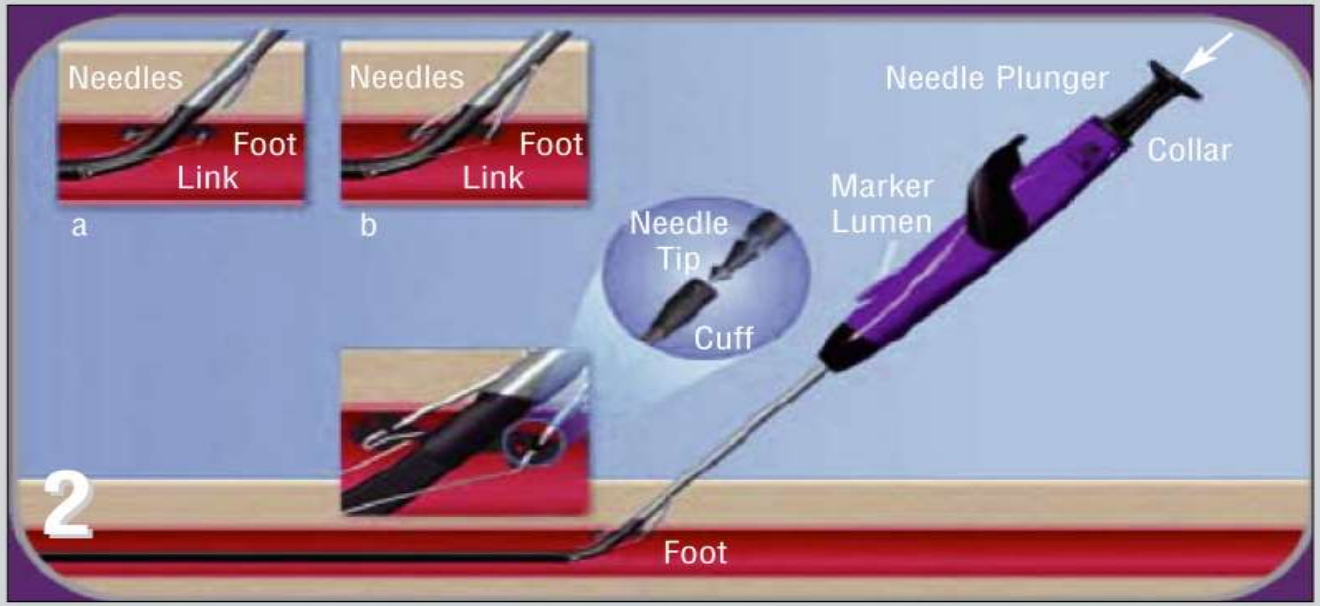
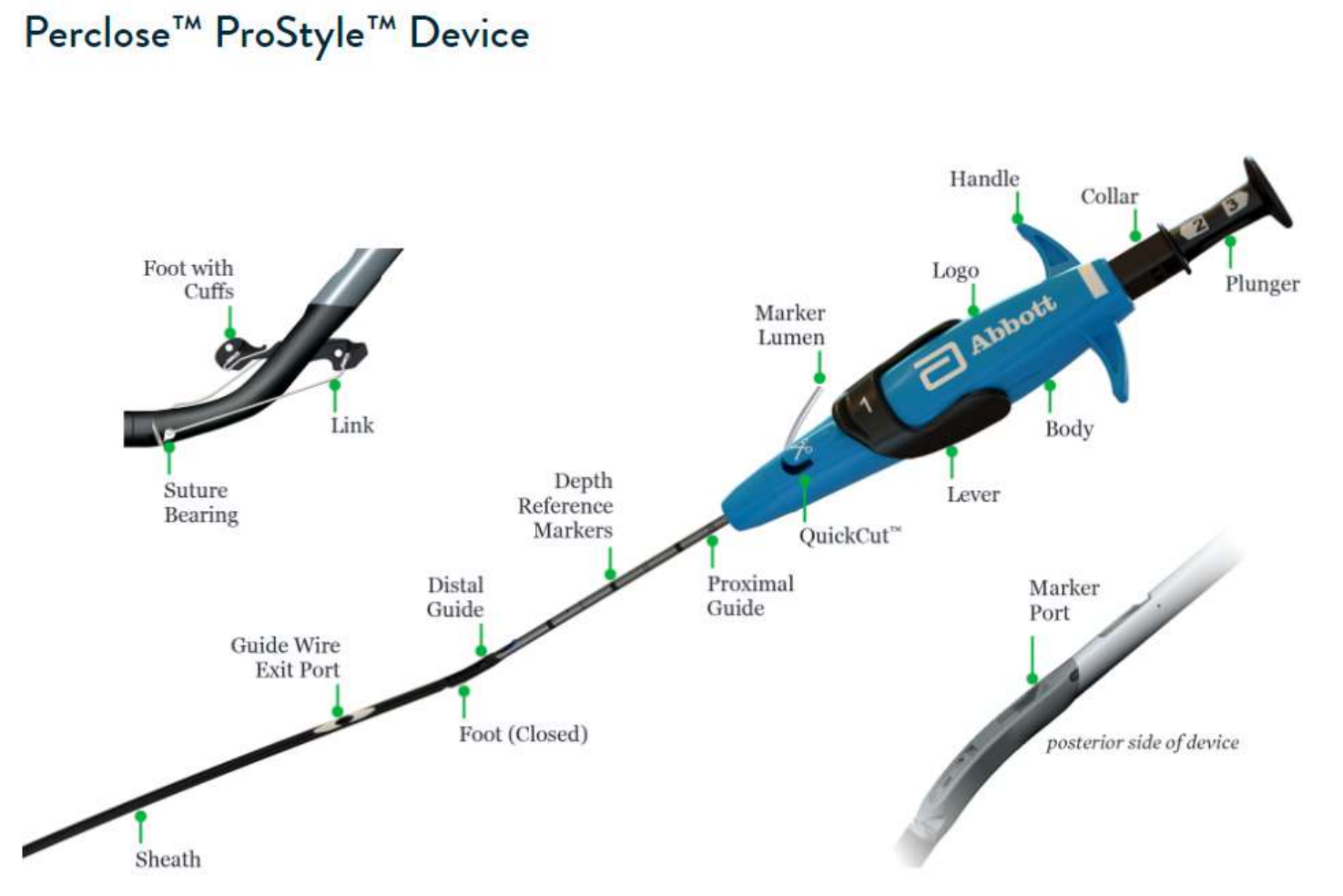


Figure 1 Perclose ProGlide Suture-Mediated Closure System: needle deployment.
Reprinted from Perclose ProGlide Suture-Mediated Closure System,[21] with permission.

- **Preclose Suture-Mediated Closure device: Sheath Size - 6 Fr**
- **Two needles & Polypropylene Monofilament**
- **Automated knot tying with pre-tied, heat set knot**

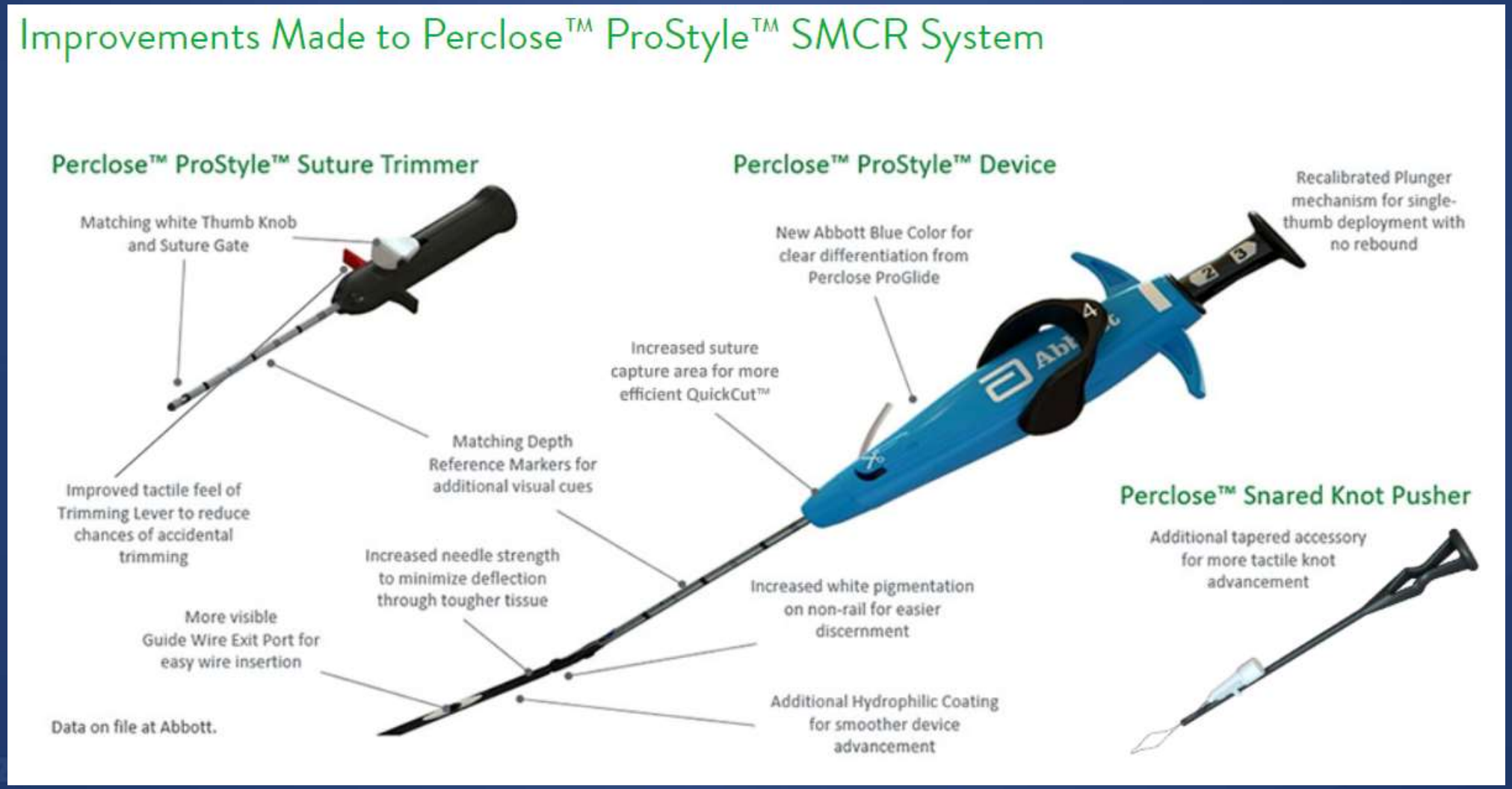
Perclose ProStyle ®

Abbott Vascular Devices



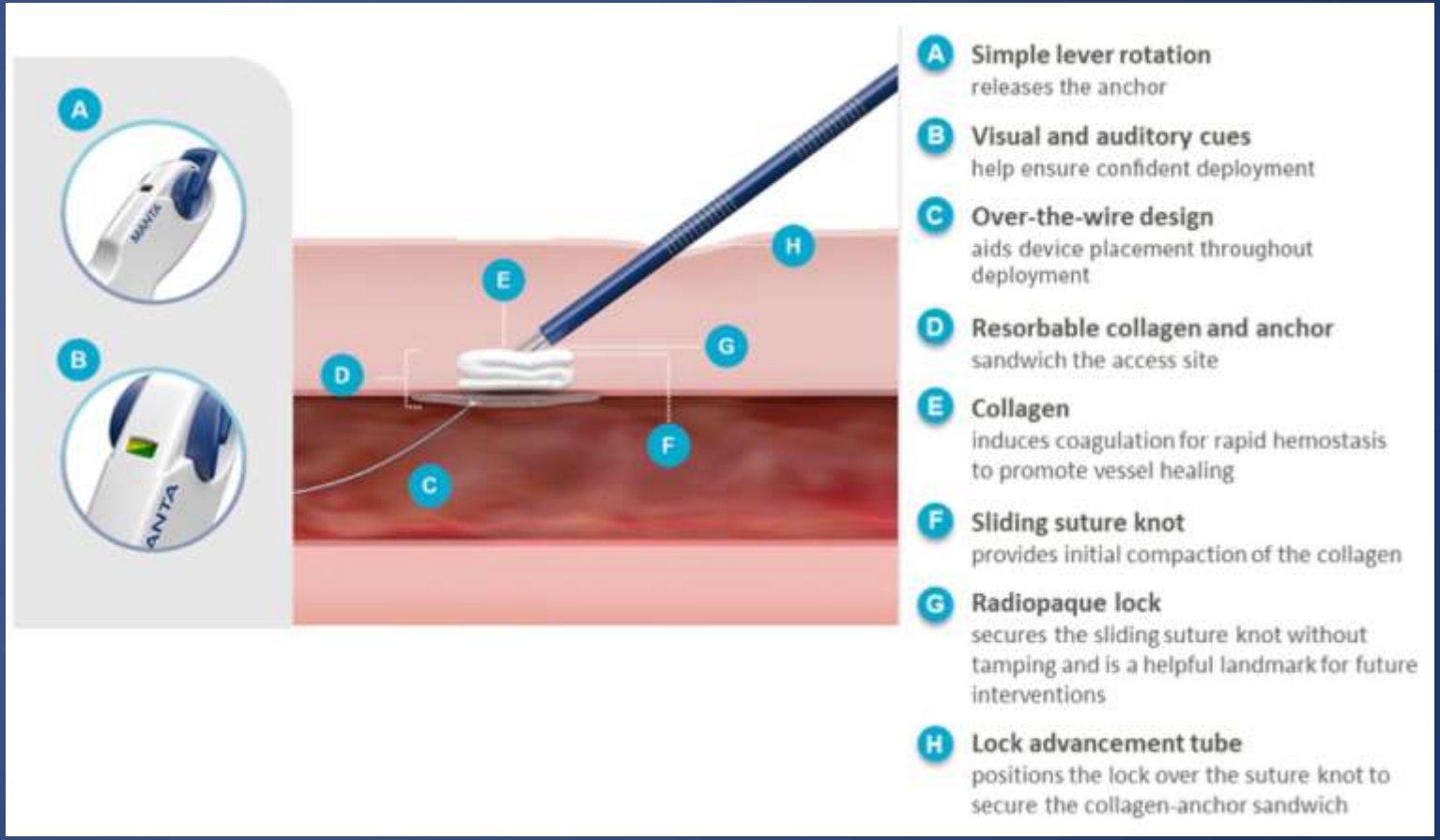
Perclose ProStyle ®

Abbott Vascular Devices

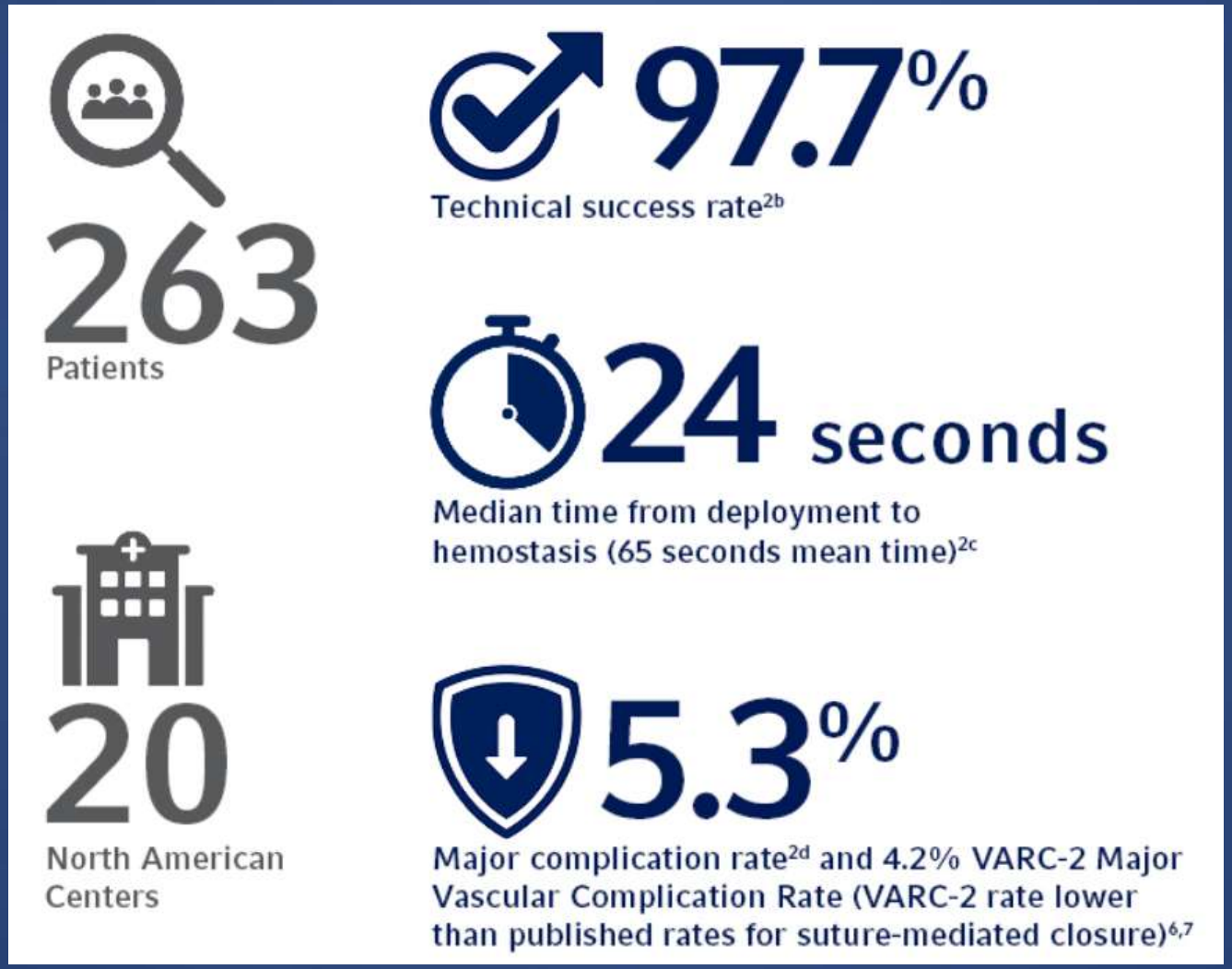


MANTA Vascular Closure

- 14 Fr and 18 Fr devices
- 8 Fr Puncture location dilator
- Intra-arterial bioresorbable toggle
- Extra-vascular bovine collagen pad
- Resorbed within 6 months



MANTA Vascular Closure



David A Wood, et al. Circ Cardiovasc Interv. 2019;12:e007258

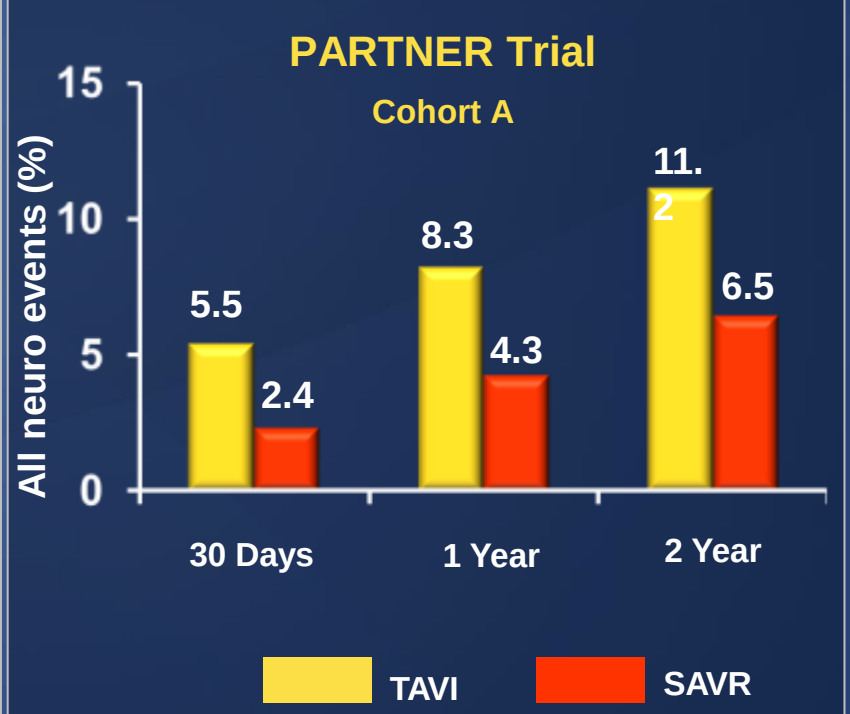
Complications

Stroke

Causes

- **Mechanical Dislodgement**
  - Catheters, Delivery system,
  - Balloon valvuloplasty, Valve depolyment
- **Thrombus Formation**
  - Inadequate anticoagulation/antiplatelet Tx
  - Stasis/Thrombus on device,
  - Apical thrombus
- **Patient Factors**
  - Age, LV dysfunction, Atrial fibrillation,
  - Pre-existing cerebrovascular disease,
  - Presence of aortic debris
- **Others**
  - Bleeding, Low output status, Air emboli

Incidence of Stroke



PARTNER trial : All Stroke (ITT)

3 year follow-up

Inoperable Cohort

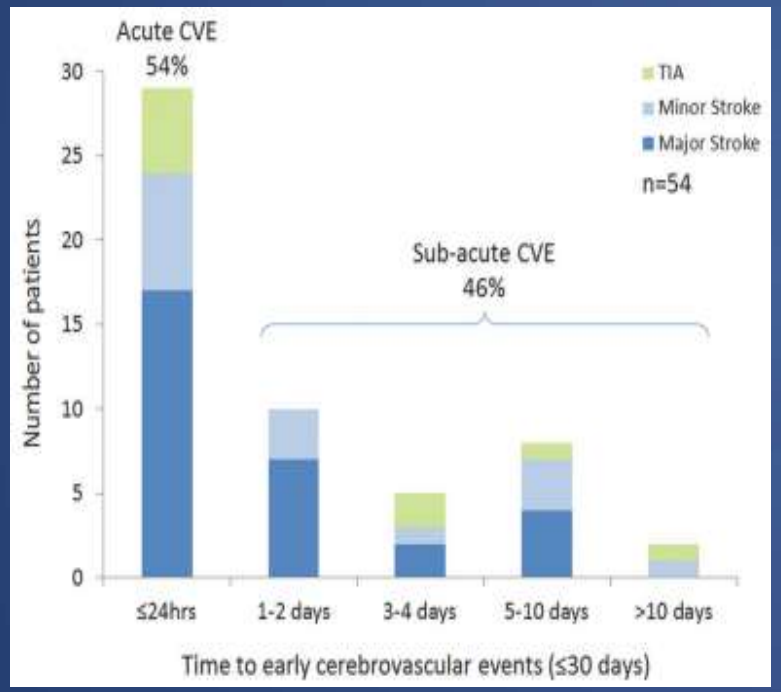
Samir R. Kapadia et al. TCT 2012

High Risk Cohort

Vinod H. Thourani et al. ACC 2013

Timing, Predictive Factors, and Prognostic Value of Stroke in TAVI

Observational study looked at stroke/TIA in 1,061 patients treated at 5 centers, January 2005-September 2011.

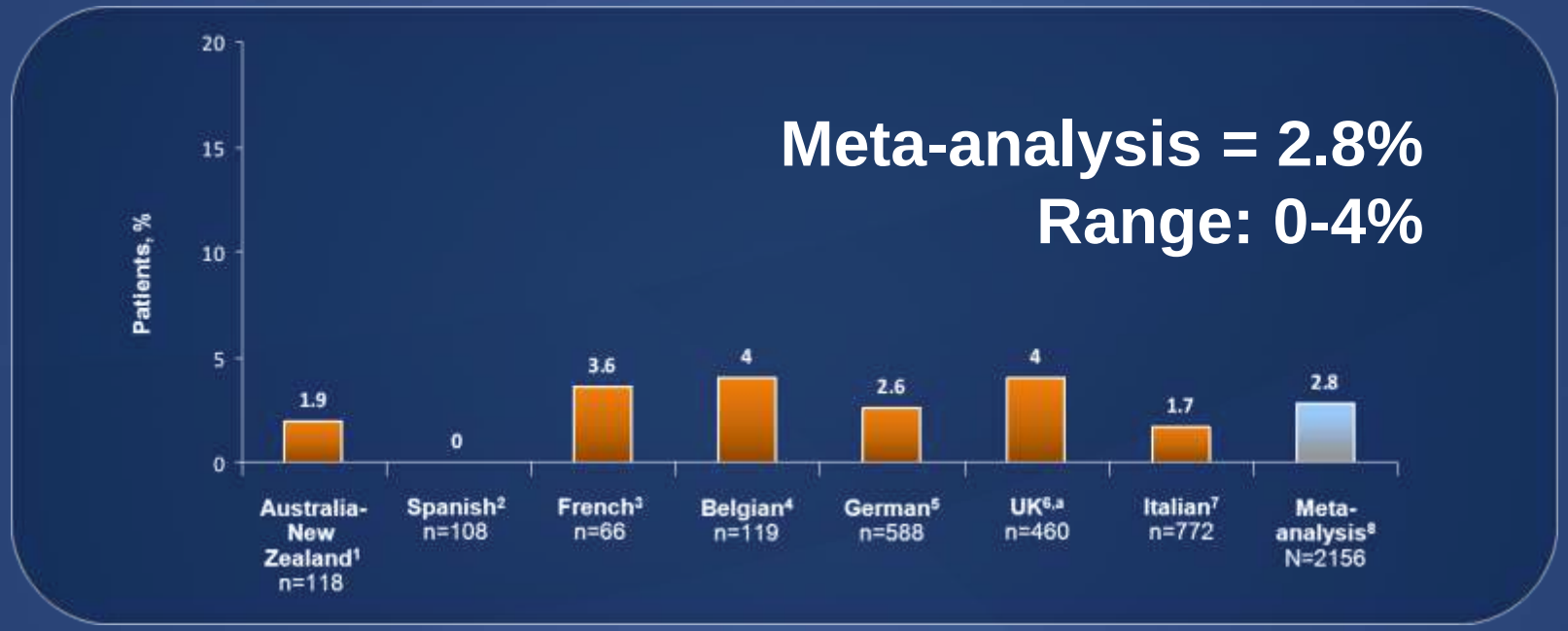


- Acute events (≤24 hrs) independently predicted by balloon postdilation and valve dislodgement/ embolization
- Subacute events (1-30 days) predicted by new onset A-fib, while late events (> 30 days) associated with chronic A-fib, PVD, and cerebrovascular disease
- Major stroke predicts mortality both early (OR 7.43; 95% CI 2.45-22.53) and late (HR 1.75; 95% CI 1.01-3.04)

Luis Nombela-Franco, et al. Circulation. 2012;126:3041-3053.

CoreValve Meta-analysis

30 day stroke rate

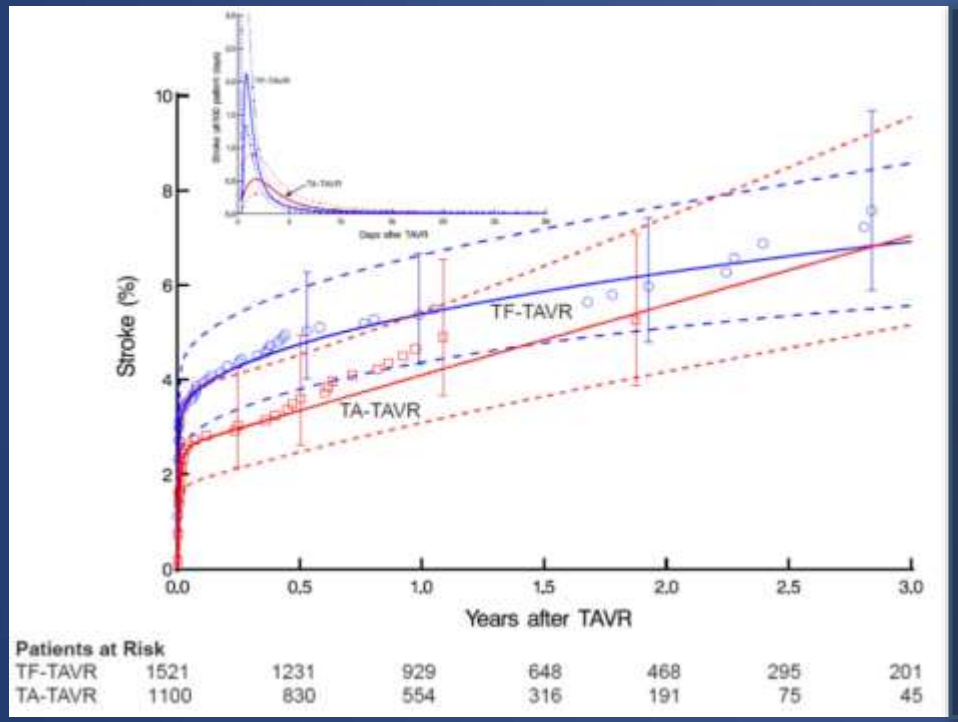


Stroke is not defined consistently across all studies.
[a]In-hospital stroke rate reported.

1. Meredith IT. The Australia-New Zealand Medtronic CoreValve® Registry: outcomes in inoperable and high risk AS patients. Presented at: TCT. 2010.
2. Avanzas P, et al. *Rev Esp Cardiol*. 2010;63:141-148.
3. Eltchaninoff H. French Registry. TAVI facts, figures and national registries. Presented at: EuroPCR; May 25-28, 2010; Paris, France.
4. Bosmans J. Belgian Registry. TAVI facts, figures and national registries. Presented at: EuroPCR; May 25-28, 2010; Paris, France.
5. Zahn R. German Registry. TAVI facts, figures and national registries. Presented at: EuroPCR; May 25-28, 2010; Paris, France.
6. Ludman P. UK Registry. TAVI facts, figures and national registries. Presented at: EuroPCR; May 25-28, 2010; Paris, France.
7. Petronio AS. Italian Registry. TAVI facts, figures and national registries. Presented at: EuroPCR; May 25-28, 2010; Paris, France.
8. Ruiz CE, et al. Weighted meta-analysis of early and late clinical outcomes after CoreValve® – TAVI in seven national registries. Presented at: EuroPCR; May 17-20, 2011; Paris, France. Analysis funded by Medtronic, Inc.

Timing, Risk Factors, Outcomes of Stroke, TIA after TAVR: PARTNER Trial

2621 participants in the PARTNER trial and continued-access registry who were followed out to 30 days, 1 year, and 3 years.



- Stroke incidence was 3.3% at 30d (of which 85% occurred within 1week)
- Rates were 3.8% at 30d, 5.4% at 1y, and 6.9% at 3y for TF-TAVR
- Higher pre-TAVR AV peak gradient was key risk factor for stroke following TF TAVR; more postdilations, pure aortic stenosis without regurgitation, more pacing runs, earlier date of procedure, and lack of DAPT were risk factors for stroke following TA TAVR

Kapadia S, et al. Circ Cardiovasc Interv. 2016;9:e002981.

Transcatheter Aortic Valve Replacement and Stroke: a comprehensive review

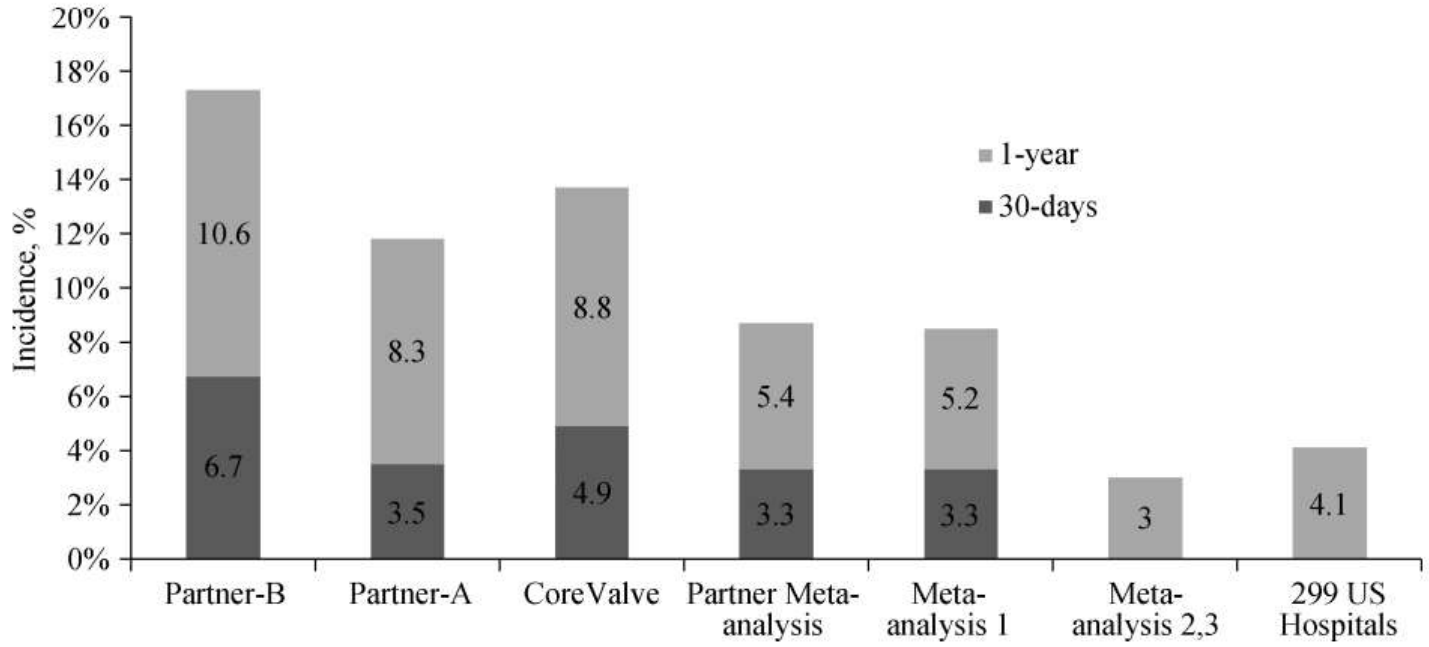
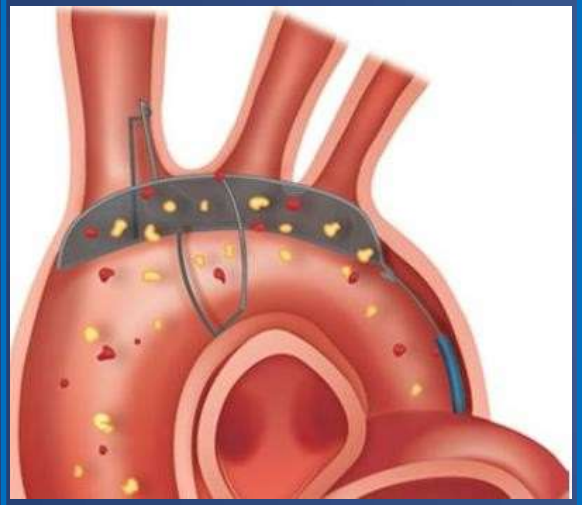


Figure 1. Incidence of stroke following TAVR in landmark studies and meta-analyses. PARTNER-B,[4] PARTNER-A,[12] CoreValve,[7] PARTNER Meta-analysis,[11] meta-analysis 1,[15] meta-analyses 2,3,[9,23] and 299 US hospitals.[24] TAVR: transcatheter aortic valve replacement.

Periklis A Davlouros, et al. J of Geriatric Cardiology 2018;15:95-104

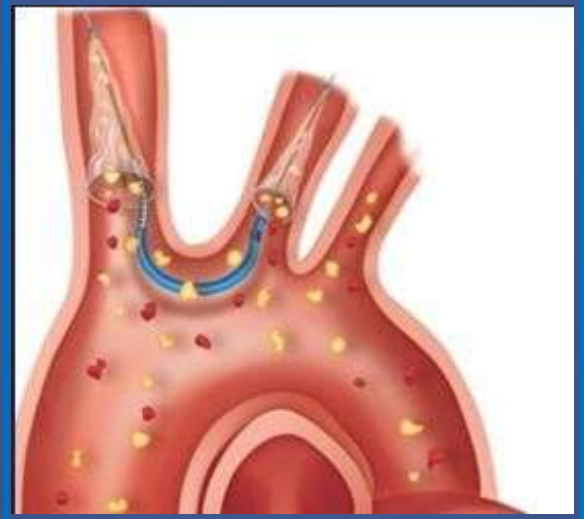
Embolic protection devices

TriGuard Embolic Deflection Device (Keystone Heart)[1]



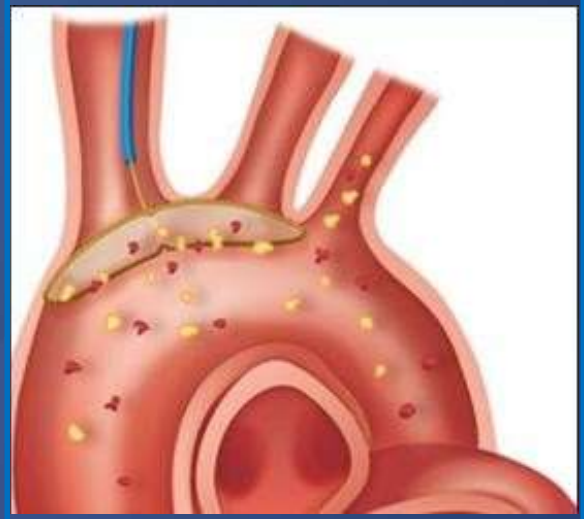
- ✓ Pore Size: 130 µm
- ✓ Delivery Sheath: 9F
- ✓ Access: Transfemoral
- ✓ Coverage: Brachiocephalic, left common carotid, left subclavian

Sentinel Cerebral Protection System (Claret Medical)[2]



- ✓ Pore Size: 140 µm
- ✓ Delivery Sheath: 6F
- ✓ Access: Brachial or radial
- ✓ Coverage: Brachiocephalic, left common carotid

Embrella Embolic Deflector System (Edwards Lifesciences)[3]

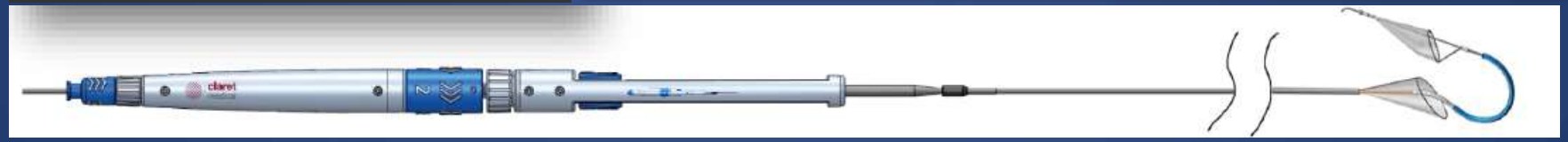


- ✓ Pore Size: 100 µm
- ✓ Delivery Sheath: 6F
- ✓ Access: Brachial
- ✓ Coverage: Brachiocephalic, left common carotid

[1]Lansky, et. al. , presented at TCT 2015; [2]Van Mieghem, et al., presented at TCT 2015;
[3]Rodes-Cabau, et al., *J Am Coll Cardiol Intv* 2014;7:1146-55

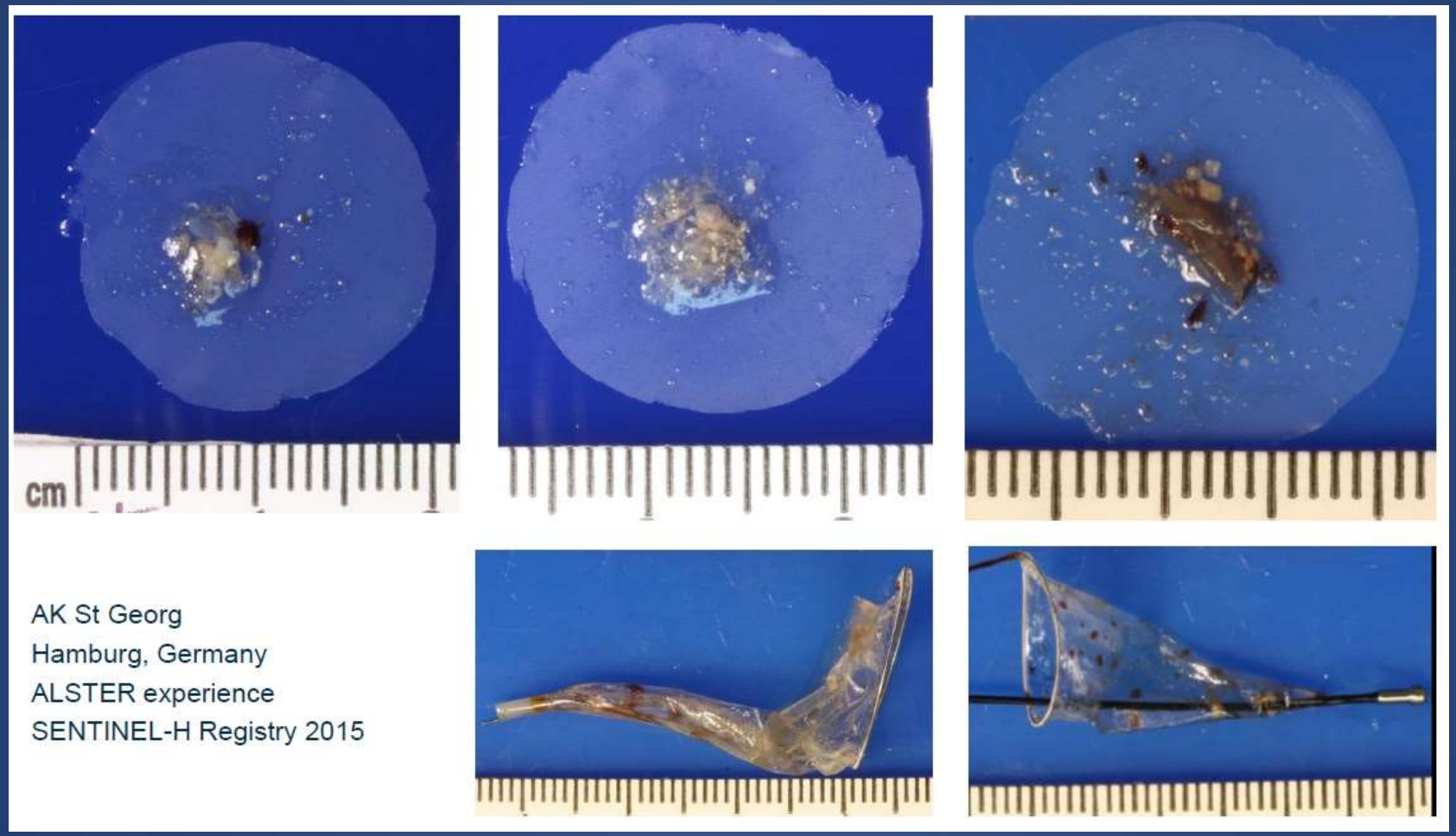
Claret Sentinel™ Cerebral Protection System (CPS)

- The only dual, independent filter (proximal and distal) cerebral embolic protection device with visible embolic debris capture and removal
- The 3rd generation of the 1st commercially available CE-marked embolic protection device
- Universal size and shape
- Deflectable compound curve sheath facilitates cannulation of LCC
- Right transradial6F sheath access using a standard 0.014” guidewire
- Filters are out of the way of TAVI delivery catheter and accessories during the TAVI procedure



Susheel Kodali, TCT 2015

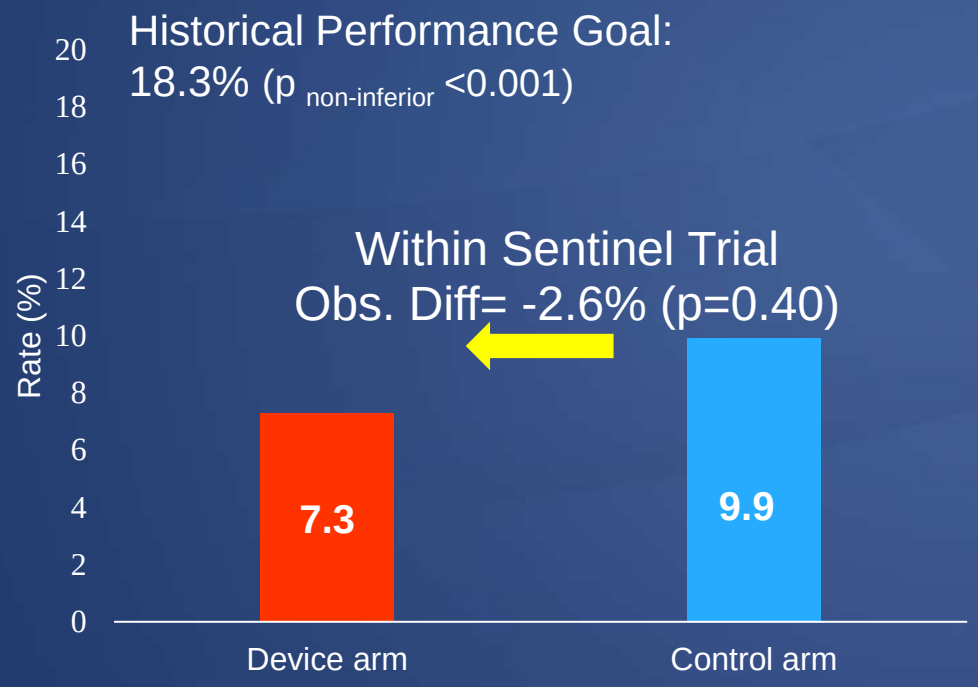
Examples of debris captured with Claret CPS



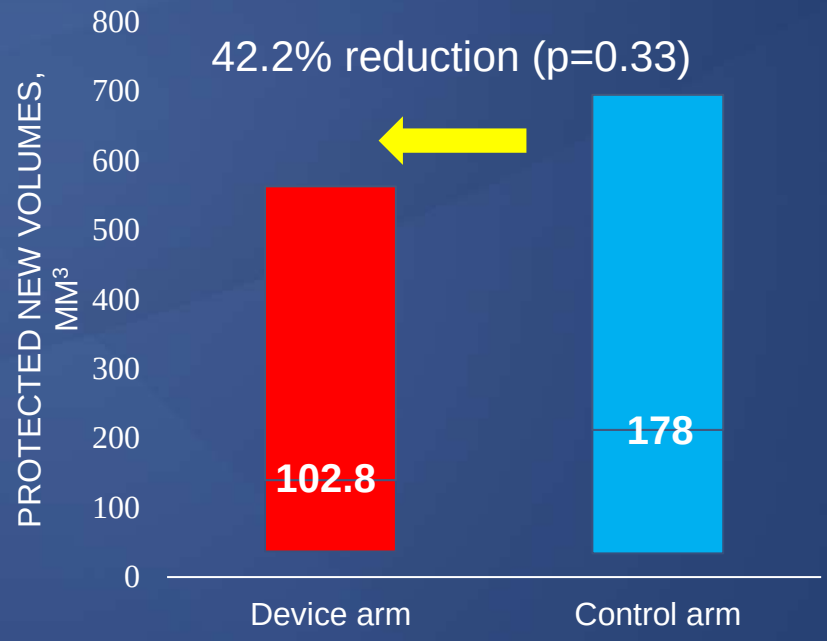
Susheel Kodali, TCT 2015

SENTINEL Trial

Primary Safety Endpoint
30-Day MACCE



Primary Efficacy Endpoint
MRI New Lesion Volume (Protected Territories)



Kapadia SR, et al. J Am Coll Cardiol. 2017;69:367–377.

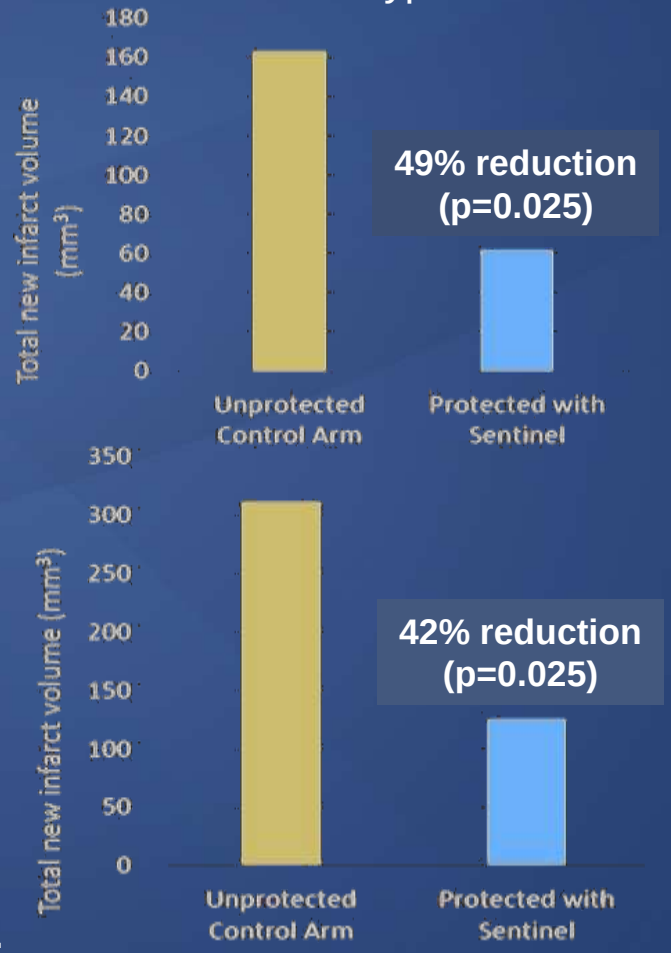
SENTINEL Trial

New Lesion Volume – Protected and All Territories

Adjusted for Baseline lesion volume, Valve Type, Interaction of Valve Type and Treatment Arm

	Mean Estimate (95% CI)	p-value
Protected Territories		
Control Arm	162.8 mm3 (107.9, 245.5)	0.0248
Sentinel Arm	83.3 mm3 (55.0, 126.1)	

	Mean Estimate (95% CI)	p-value
All Territories		
Control Arm	311.1 mm3 (212.2, 456.3)	0.0500
Sentinel Arm	180.6 mm3 (122.7, 265.8)	



Kapadia SR, et al. J Am Coll Cardiol. 2017;69:367–377.

Cerebral Embolic Protection and Outcomes of TAVR

Observational study from STS/ACC TVT Registry

Table 2. Unadjusted Outcomes

	EPD usage (N=12 409)	No EPD usage (N=110 777)	Odds ratio (95% CI)	*P* value
Primary end point				
In-hospital stroke, n/N (%)	158/12 409 (1.3)	1716/110 777 (1.5)	0.82 (0.65–1.03)	0.083
Secondary end points				
In-hospital stroke or death, n/N (%)	245/12 409 (2.0)	2876/110 777 (2.6)	0.76 (0.62–0.92)	0.006
In-hospital stroke or TIA, n/N (%)	183/12 409 (1.5)	1872/110 777 (1.7)	0.87 (0.72–1.06)	0.160
In-hospital death, n/N (%)	99/12 409 (0.8)	1317/110 777 (1.2)	0.67 (0.51–0.88)	0.005
Device success, n/N (%)	11 745/12 120 (96.9)	107 072/110 090 (97.3)	0.88 (0.62–1.25)	0.482
In-hospital major bleeding, n/N (%)	491/12 266 (4.0)	4808/108 858 (4.4)	0.90 (0.75–1.09)	0.277
30-day stroke, n/N (%)	216/11 682 (1.8)	2224/102 919 (2.2)	0.85 (0.7–1.04)	0.123
30-day death, n/N (%)	162/11 658 (1.4)	2297/102 877 (2.2)	0.62 (0.49–0.78)	<0.001
Falsification end point				
GI/GU bleeding, n/N (%)	58/12 409 (0.5)	501/110 777 (0.5)	1.03 (0.75–1.42)	0.837

Odds ratios, 95% CIs, and Wald Chi-square *P* values obtained from unadjusted generalized estimating equations, accounting for with clustering by site. EPD indicates embolic protection device; GI/GU, gastrointestinal/genitourinary; and TIA, transient ischemic attack.

Neel M. Butala, et al. Circulation. 2021;143:2229–2240.

Cerebral Embolic Protection and Outcomes of TAVR

Observational study from STS/ACC TVT Registry

Table 3. Adjusted Association of Post–Transcatheter Aortic Valve Replacement Outcomes With Use of Cerebral Embolic Protection During Valve Implantation

	Instrumental variable analysis model					Propensity score–based model				
	EPD (%)	No EPD (%)	Absolute risk difference, % (95% CI)	Adjusted relative risk (95% CI)	*P* value	EPD (%)	No EPD (%)	Absolute risk difference, % (95% CI)	Adjusted odds ratio (95% CI)	*P* value
Primary end point										
In-hospital stroke	1.39	1.54	−0.15 (−0.49 to 0.20)	0.90 (0.68–1.13)	0.414	1.3	1.58	−0.28 (−0.52 to −0.03)	0.82 (0.69–0.97)	0.018
Secondary end points										
In-hospital stroke or death	2.38	2.55	−0.17 (−0.61 to 0.28)	0.93 (0.76–1.11)	0.466	2.14	2.52	−0.38 (−0.69 to −0.02)	0.84 (0.73–0.98)	0.026
In-hospital stroke or TIA	1.60	1.68	−0.07 (−0.44 to 0.29)	0.96 (0.74–1.17)	0.696	1.47	1.69	−0.22 (−0.46 to −0.05)	0.87 (0.75–1.01)	0.073
In-hospital death	1.07	1.16	−0.09 (−0.39 to 0.22)	0.92 (0.66–1.19)	0.576	0.94	1.09	−0.15 (−0.37 to 0.08)	0.86 (0.66–1.1)	0.231
Device success	97.03	97.23	−0.2 (−0.67 to 0.27)	1.00 (0.99–1.00)	0.405	97.37	97.34	0.03 (−0.70 to 0.79)	1.01 (0.76, 1.35)	0.934
In-hospital major bleeding	4.76	4.33	0.43 (−0.15 to 1.02)	1.10 (0.97–1.24)	0.148	4.68	4.33	0.35 (−0.27 to 0.76)	1.09 (0.95–1.24)	0.218
30-day stroke	1.97	2.14	−0.17 (−0.60 to 0.25)	0.92 (0.72–1.12)	0.416	1.92	2.24	−0.32 (−0.61 to −0.01)	0.85 (0.73–0.99)	0.038
30-day mortality	1.85	2.19	−0.34 (−0.76 to 0.08)	0.84 (0.65–1.04)	0.114	1.7	2.16	−0.46 (−0.78 to −0.14)	0.78 (0.64–0.95)	0.014
Falsification end point										
GI/GU bleeding	0.59	0.44	0.16 (−0.04 to 0.35)	1.34 (0.91–1.80)	0.11	0.58	0.46	0.13 (−0.05 to 0.35)	1.29 (0.92–1.81)	0.144

Neel M. Butala, et al. Circulation. 2021;143:2229–2240.

Cerebral Embolic Protection During TAVR

A Clinical Event Meta-Analysis

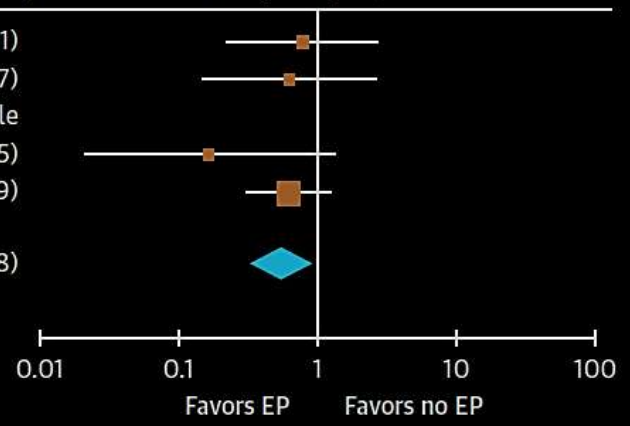
FIGURE 1 Clinical Outcomes in Patients Undergoing TAVR With Versus Without Embolic Protection Devices

Death or stroke

Study or Subgroup	Embolic protection Events	Total	No embolic protection Events	Total	Weight	Risk Ratio M-H, Fixed (95% CI)
CLEAN-TAVI	4	50	5	50	15.9%	0.80 (0.23-2.81)
DEFLECT-III	3	46	4	39	13.7%	0.64 (0.15-2.67)
EMBOL-X	0	14	0	16		Not estimable
MISTRAL-C	1	32	6	33	18.7%	0.17 (0.02-1.35)
SENTINEL	16	234	12	111	51.7%	0.63 (0.31-1.29)
Total (95% CI)		376		249	100.0%	0.57 (0.33-0.98)
Total events	24		27			

Heterogeneity: $Chi^2 = 1.68$, $df = 3$ ($P = 0.64$); $I^2 = 0\%$

Test for overall effect: $Z = 2.01$ ($P = 0.04$)

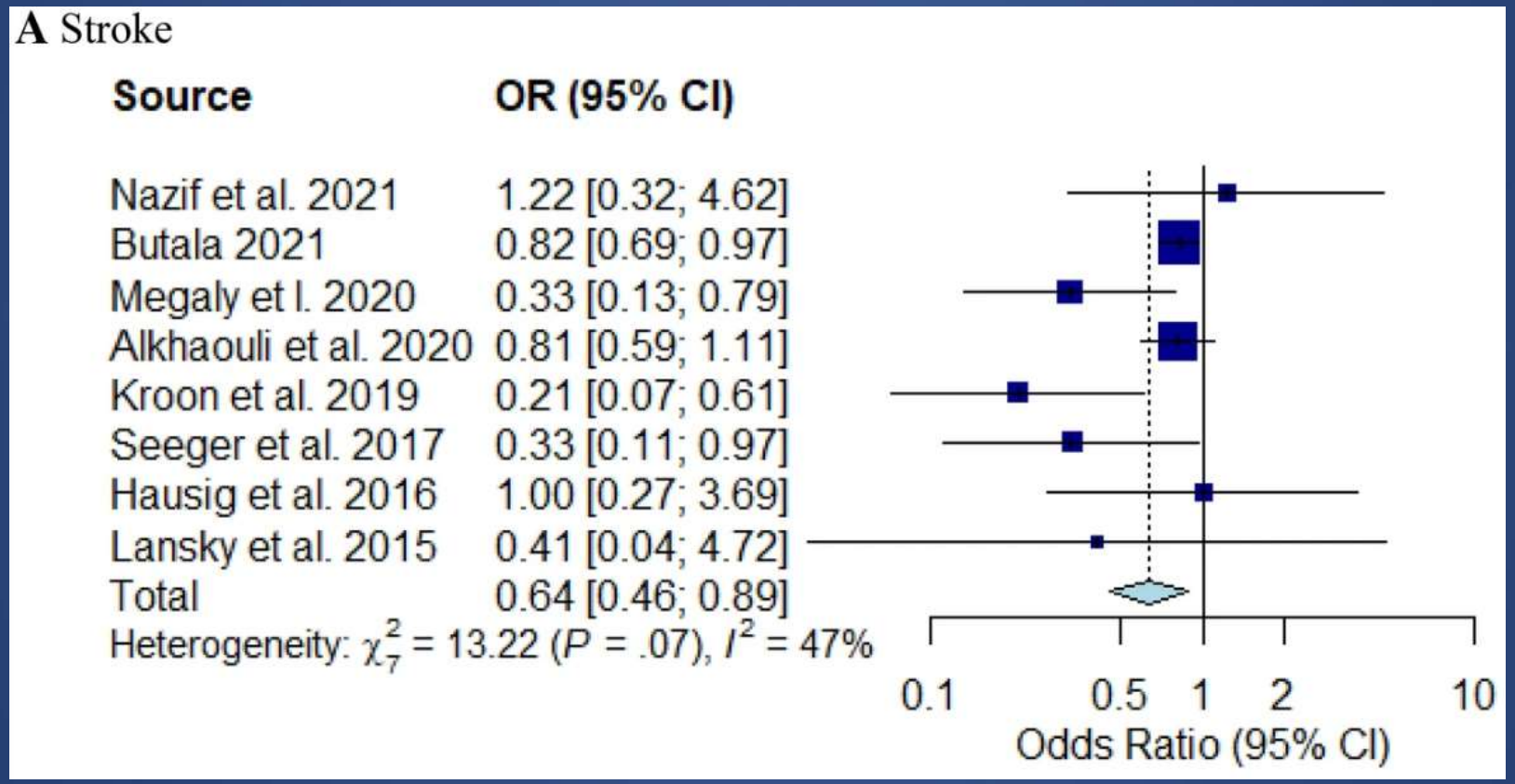


Pooled effect estimates for the risk of death or stroke according to the use of cerebral embolic protection versus not during TAVR. CI = confidence interval; CLEAN-TAVI = Claret Embolic Protection and TAVI; DEFLECT-III = A Prospective, Randomized Evaluation of the TriGuard HDH Embolic Deflection Device During TAVI; EP = embolic protection; M-H = Mantel-Haenszel; MISTRAL-C = MRI Investigation With Claret; SENTINEL = Cerebral Protection in Transcatheter Aortic Valve Replacement; TAVR = transcatheter aortic valve replacement.

Giustino G, et al. J Am Coll Cardiol. 2017 Jan 31;69(4):465-466

Safety and efficacy of Cerebral Embolic Protection device undergoing TAVR

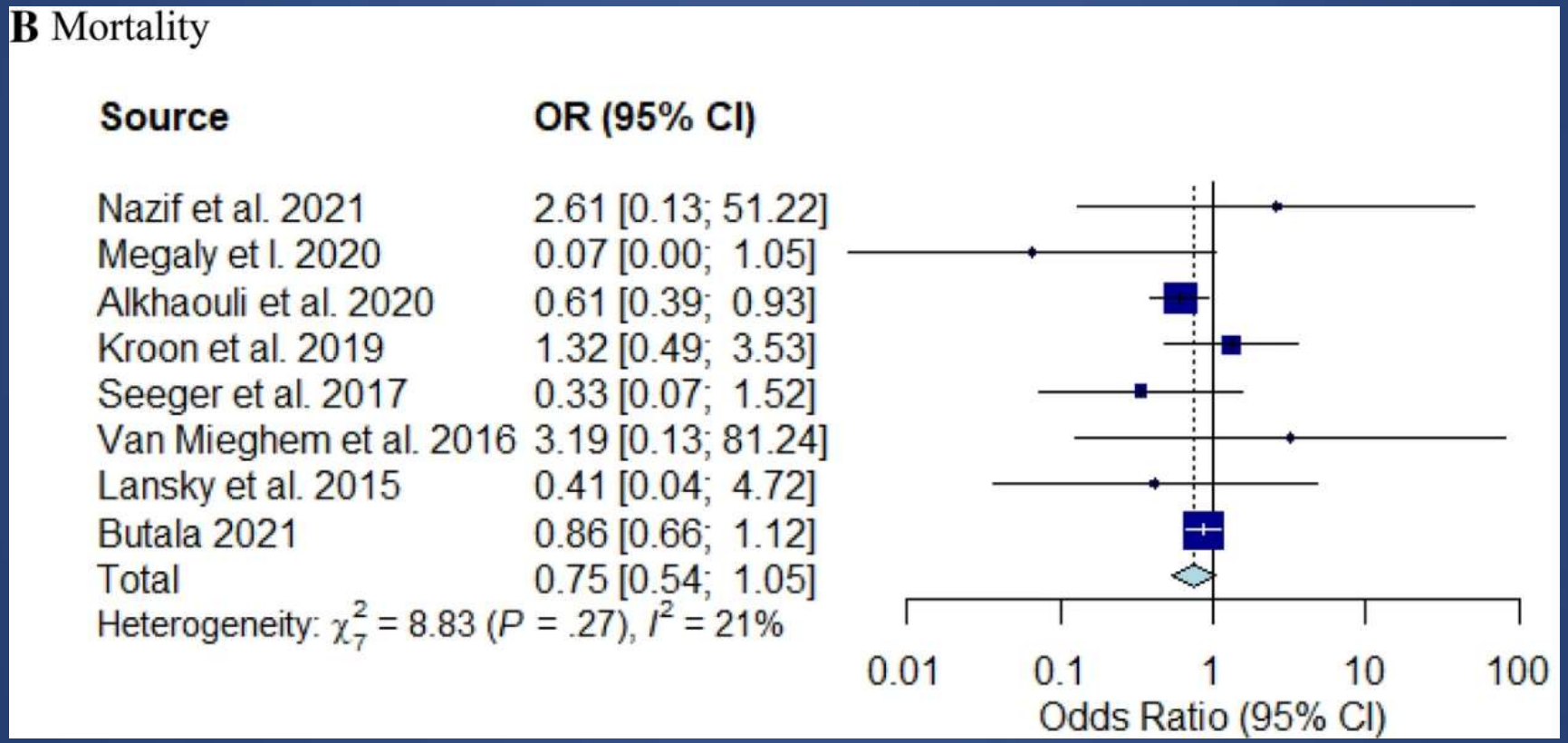
A meta-analysis of in-hospital outcomes



Junichi Shimamura et al. Cardiovasc Interv Ther. 2022;37(3):549-557

Safety and efficacy of Cerebral Embolic Protection device undergoing TAVR

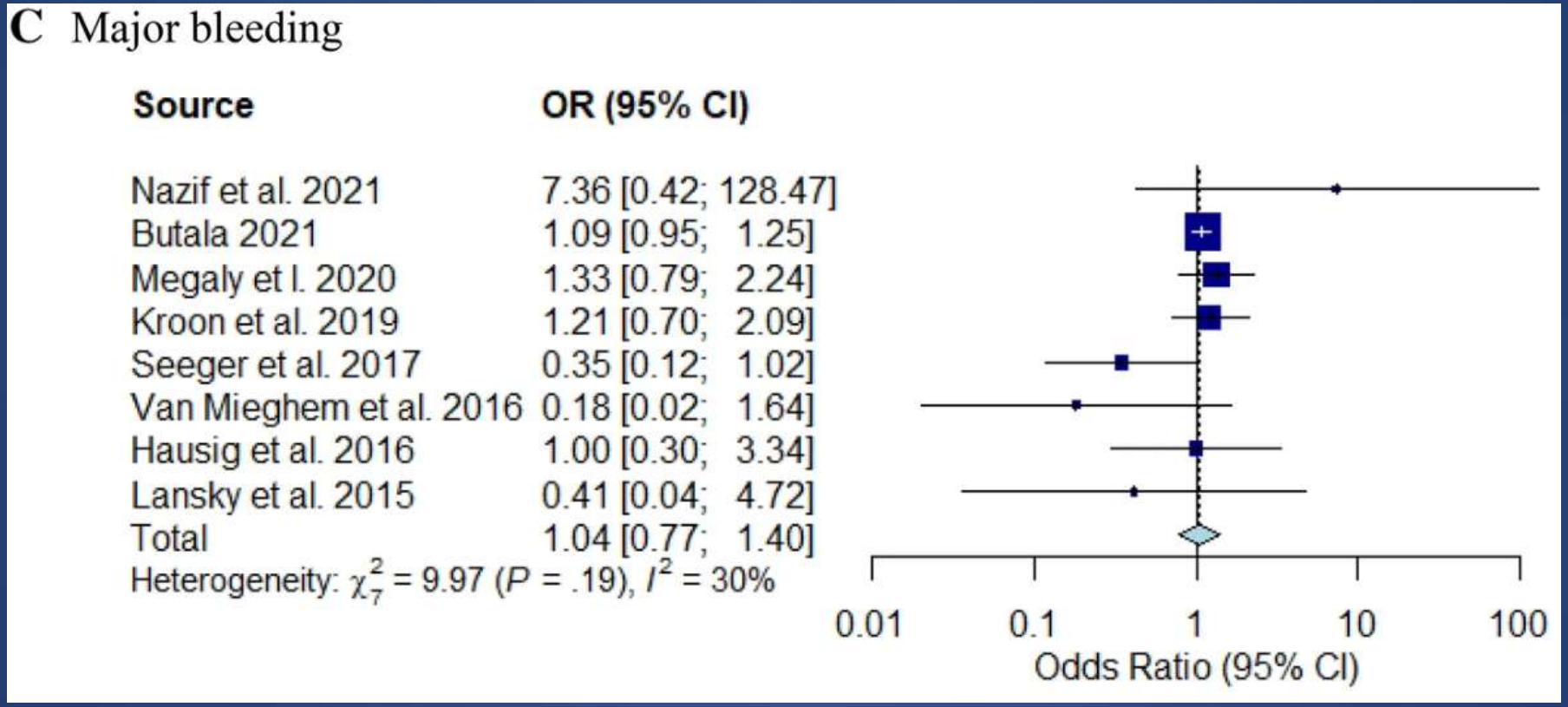
A meta-analysis of in-hospital outcomes



Junichi Shimamura et al. Cardiovasc Interv Ther. 2022;37(3):549-557

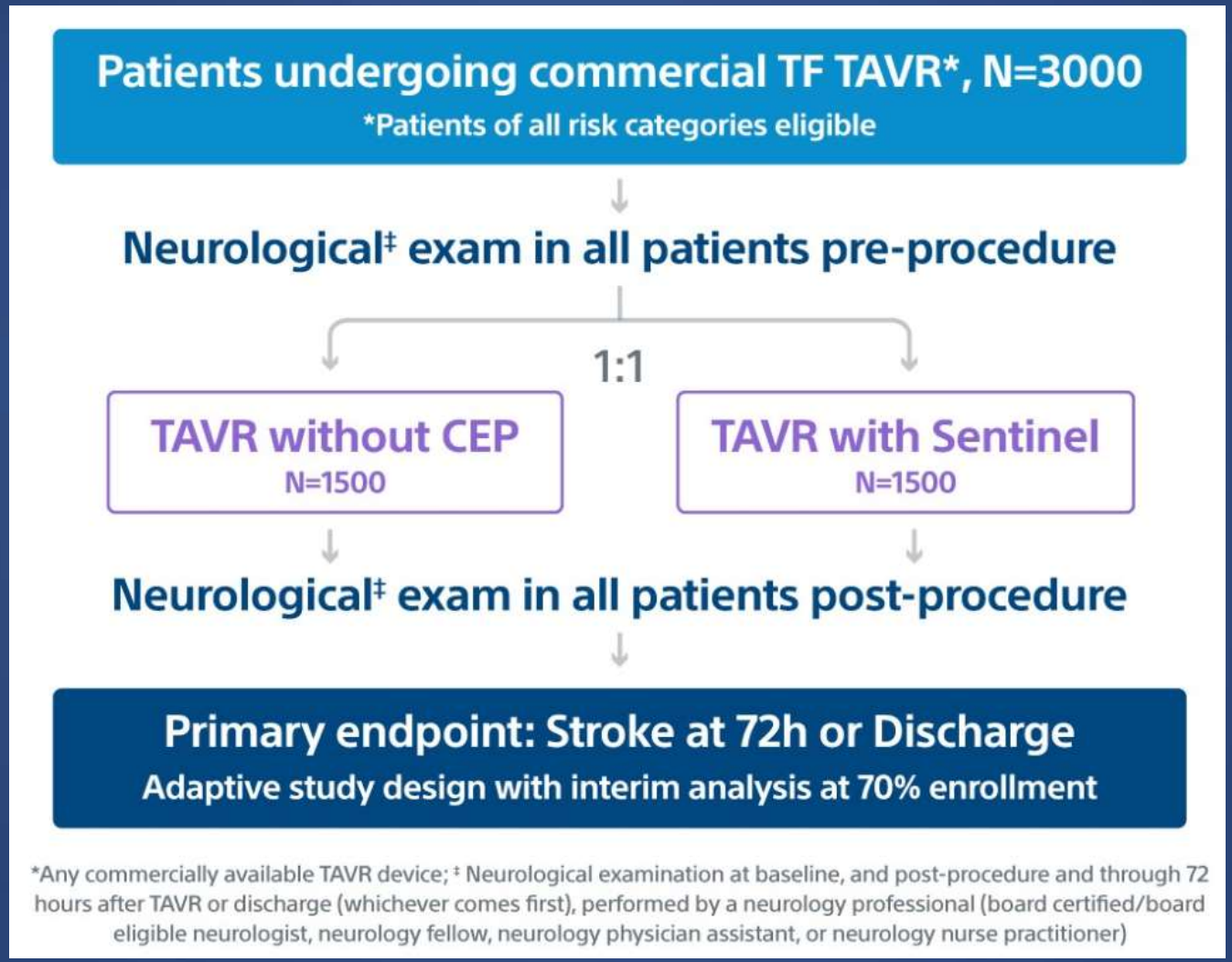
Safety and efficacy of Cerebral Embolic Protection device undergoing TAVR

A meta-analysis of in-hospital outcomes

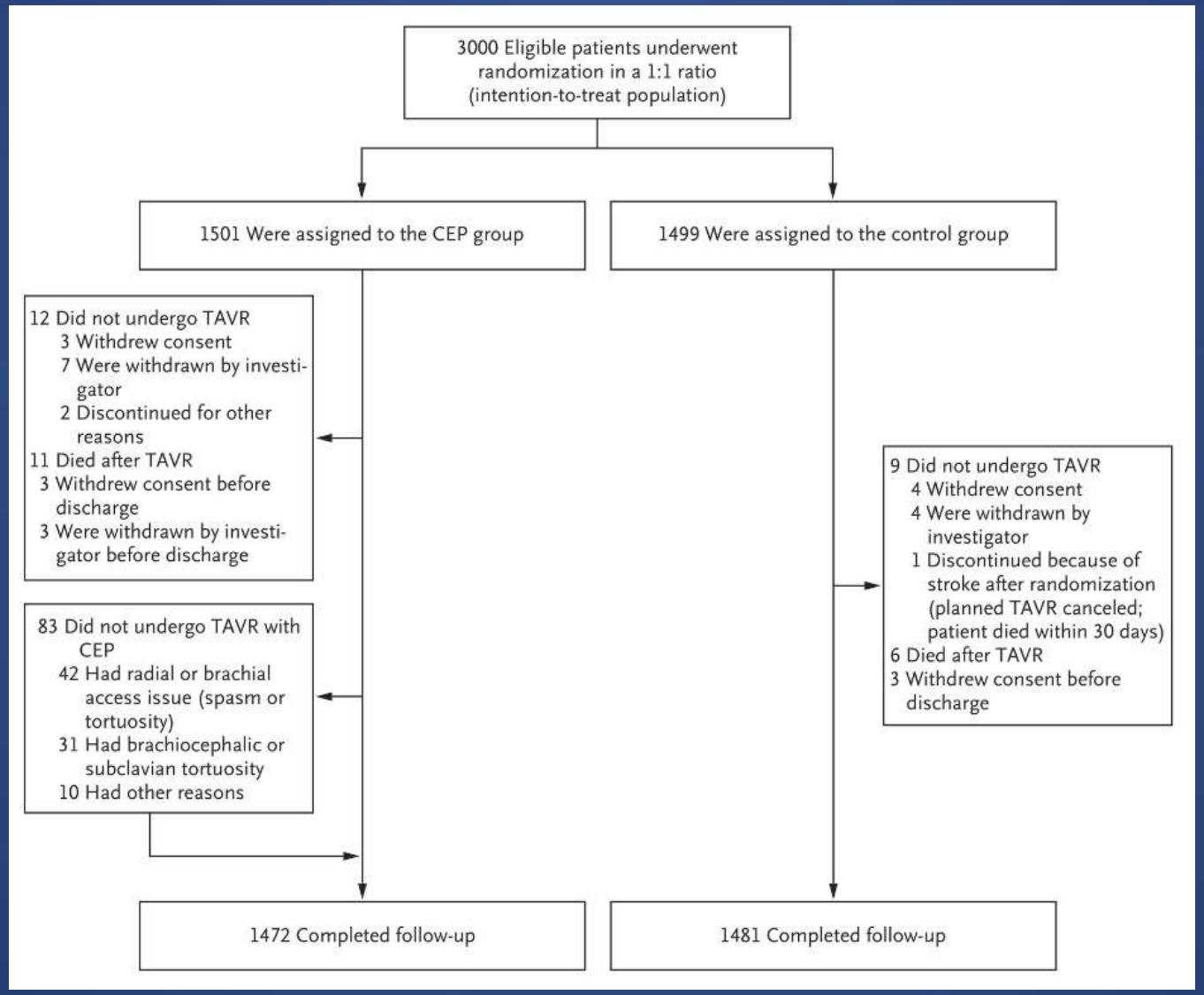


Junichi Shimamura et al. Cardiovasc Interv Ther. 2022;37(3):549-557

PROTECTED TAVR Trial



PROTECTED TAVR Trial



PROTECTED TAVR Trial

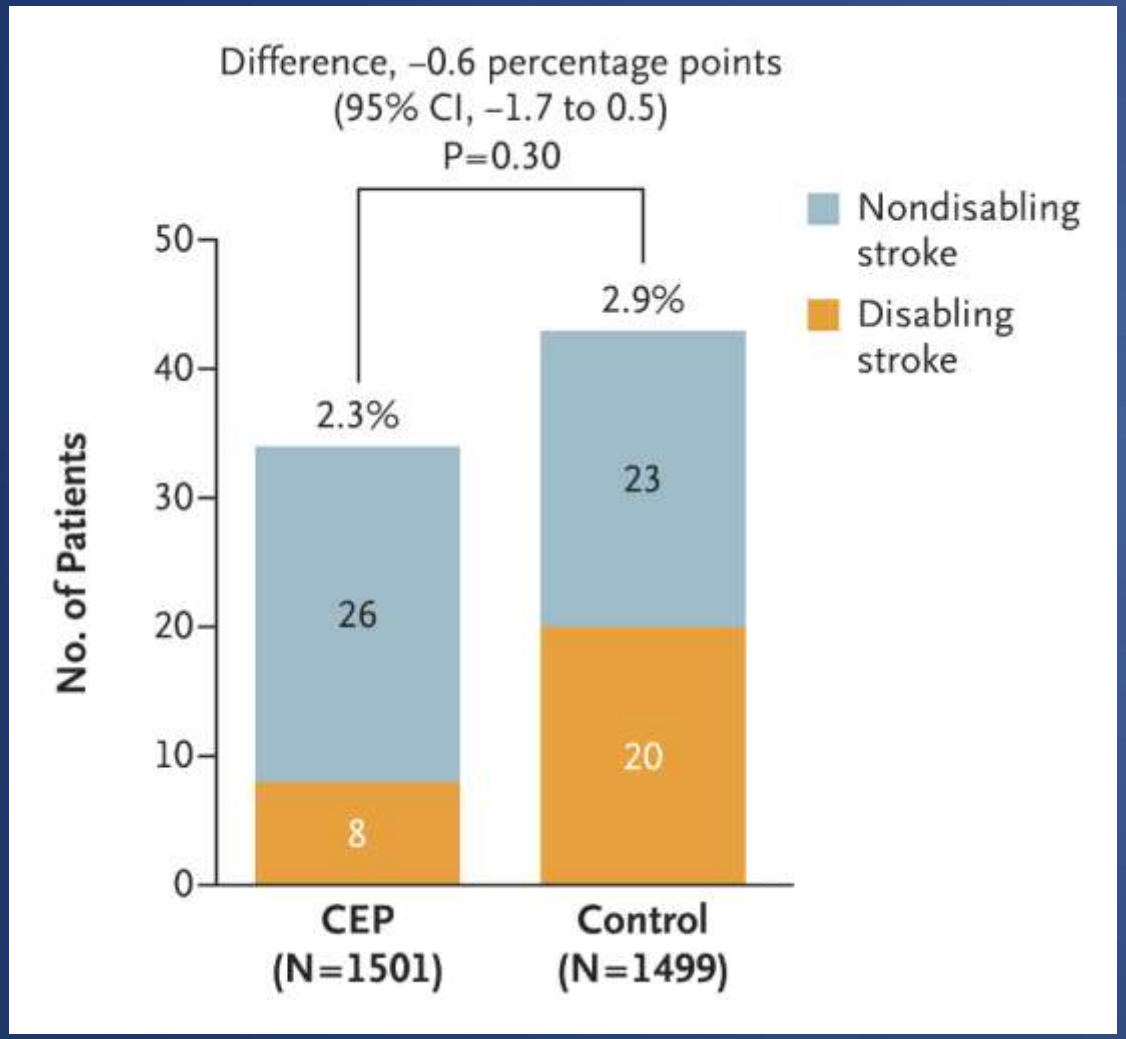


Table 2. Clinical and Neurologic Outcomes within 72 Hours after TAVR or before Discharge.*

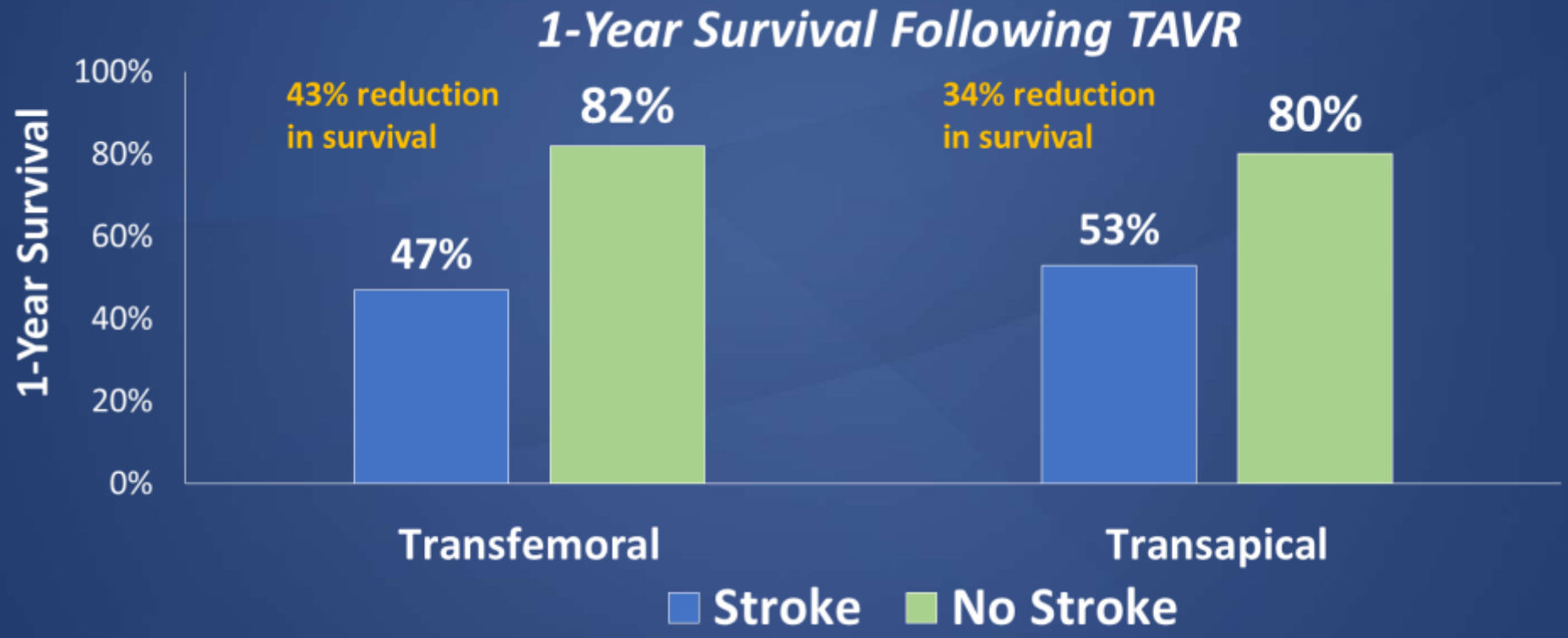
Outcome	CEP (N=1501)	Control (N=1499)	Difference (95% CI)†
Clinical			
Primary end point: stroke — no. (%)	34 (2.3)	43 (2.9)	−0.6 (−1.7 to 0.5)
Disabling	8 (0.5)	20 (1.3)	−0.8 (−1.5 to −0.1)
Ischemic	6 (0.4)	17 (1.1)	−0.7 (−1.4 to −0.1)
Hemorrhagic	2 (0.1)	3 (0.2)	−0.1 (−0.4 to 0.2)
Nondisabling	26 (1.7)	23 (1.5)	0.2 (−0.7 to 1.1)
Ischemic	26 (1.7)	23 (1.5)	0.2 (−0.7 to 1.1)
Hemorrhagic	0	0	0
Death — no. (%)			
Any cause	8 (0.5)	4 (0.3)	0.3 (−0.2 to 0.7)
Cardiovascular cause	8 (0.5)	4 (0.3)	0.3 (−0.2 to 0.7)
Noncardiovascular cause	0	0	0
Safety composite end point: death from any cause or stroke — no. (%)	41 (2.7)	45 (3.0)	−0.3 (−1.5 to 0.9)
Neurologic composite end point: stroke, transient ischemic attack, or delirium — no. (%)	46 (3.1)	55 (3.7)	−0.6 (−1.9 to 0.7)
Stroke — no. (%)	34 (2.3)	43 (2.9)	−0.6 (−1.7 to 0.5)
Transient ischemic attack — no. (%)	1 (0.1)	2 (0.1)	−0.1 (−0.3 to 0.2)
Delirium — no. (%)	12 (0.8)	11 (0.7)	0.1 (−0.6 to 0.7)
Major or minor vascular complication at the CEP access site — no. (%)	1 (0.1)	0	0.1 (−0.1 to 0.2)
Stage 2 or 3 acute kidney injury ≤72 hours after TAVR — no. (%)	8 (0.5)	7 (0.5)	0.1 (−0.4 to 0.6)
Neurologic			
NIHSS total score‡	0.4±1.8	0.4±1.2	0.1 (−0.1 to 0.2)
Modified Rankin scale score			
Mean score§	0.6±1.1	0.6±1.1	0.0 (−0.1 to 0.1)
Score of 0–1 — no./total no. (%)	1221/1468 (83.2)	1247/1473 (84.7)	−1.5 (−4.1 to 1.2)‡
Score of ≥2 — no./total no. (%)	247/1468 (16.8)	226/1473 (15.3)	1.5 (−1.2 to 4.1)‡

Stroke after SAVR vs. Transfemoral TAVR

from the PARTNER Trial

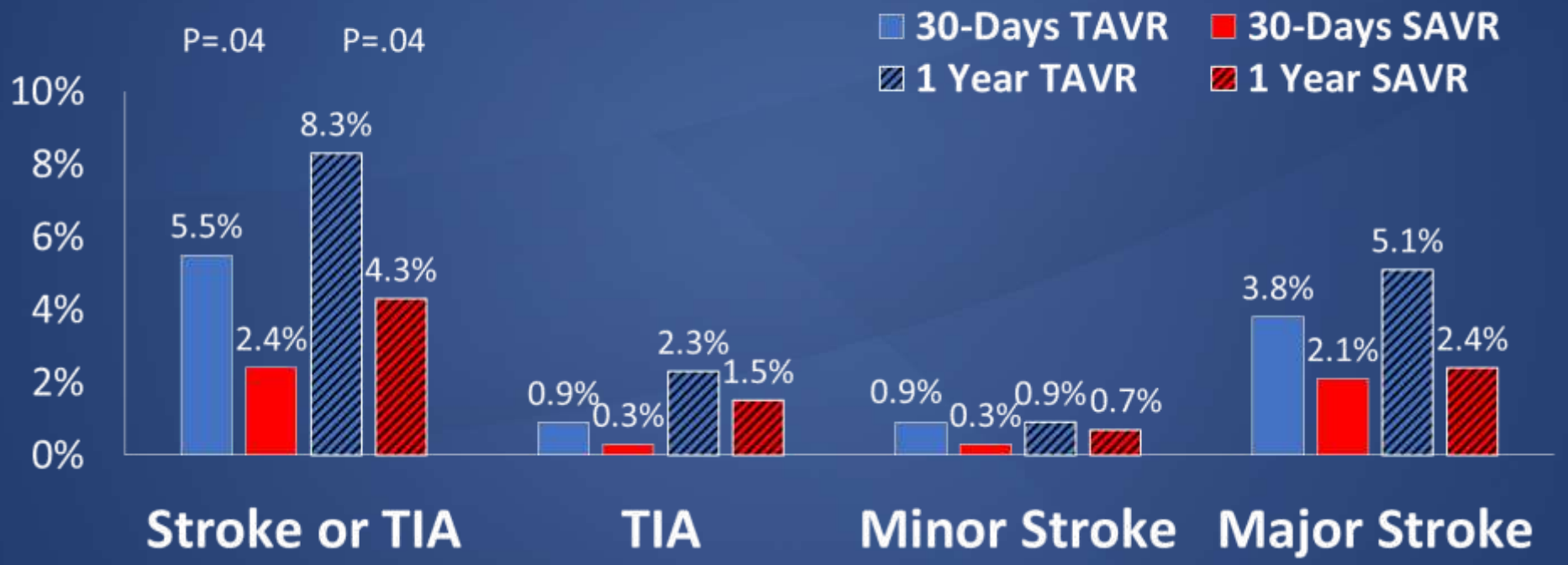
Samir R. Kapadia et al, J Am Coll Cardiol. 2018;72:2415–26.

Stroke is Associated with a Major Reduction in 1-Year Survival after TAVR



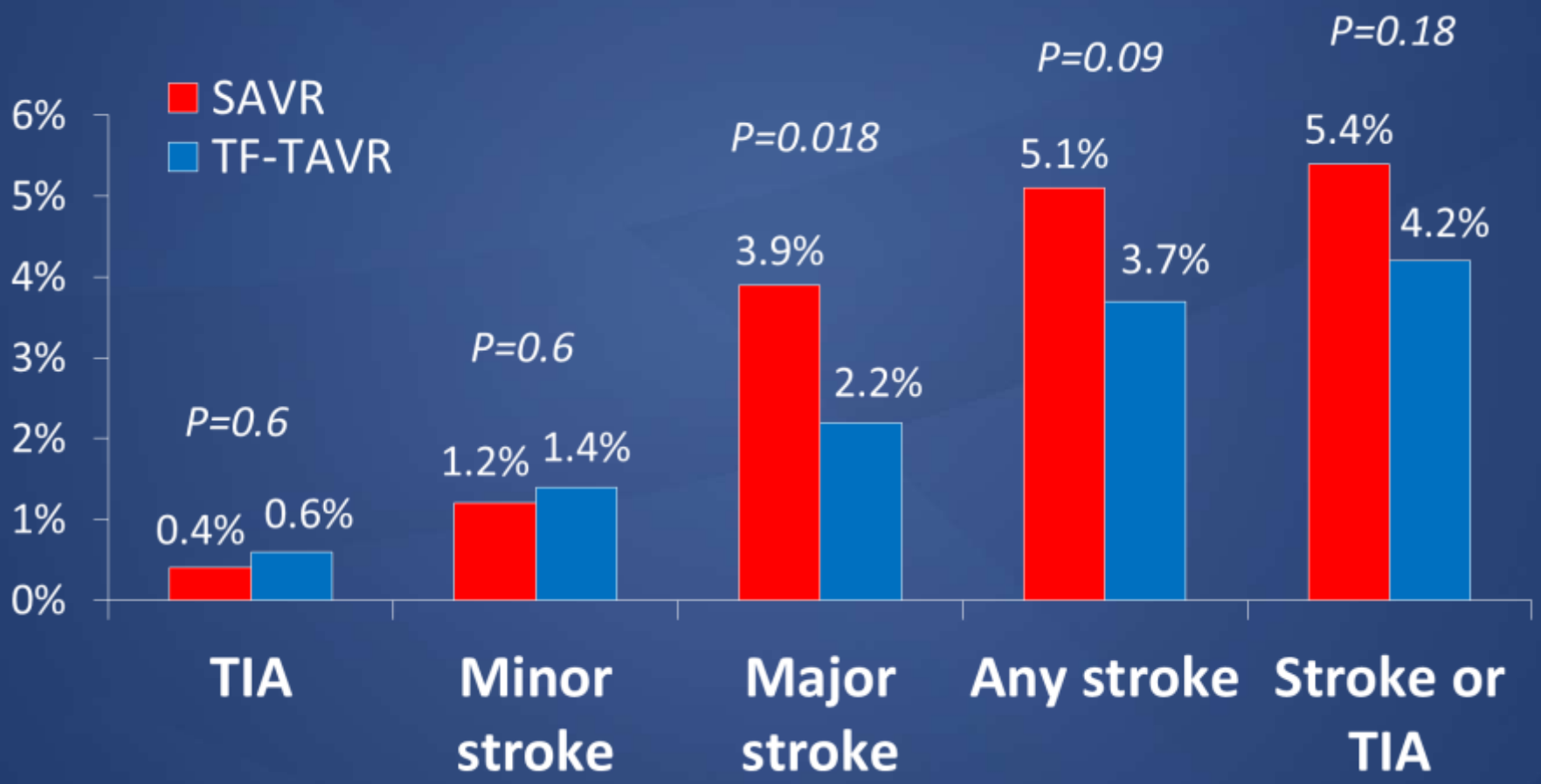
Kapadia et al. Circ Cardiovasc Interv. 2016

PARTNER 1A Raised Concern of Increased Neurologic Risk of TAVR



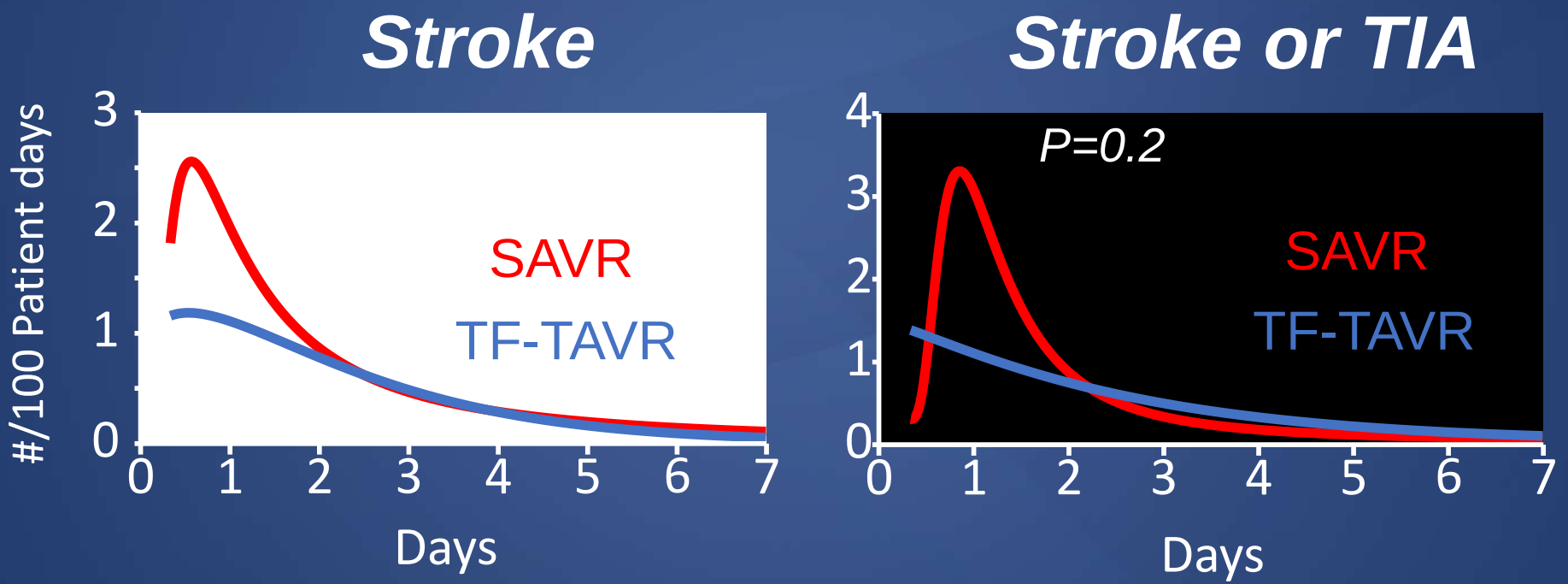
Smith et al. N Engl J Med. 2011; 364:2187-98

SAVR vs. TF-TAVR
30-Day Neurologic Events



Early Phase Risk (<7 Days)

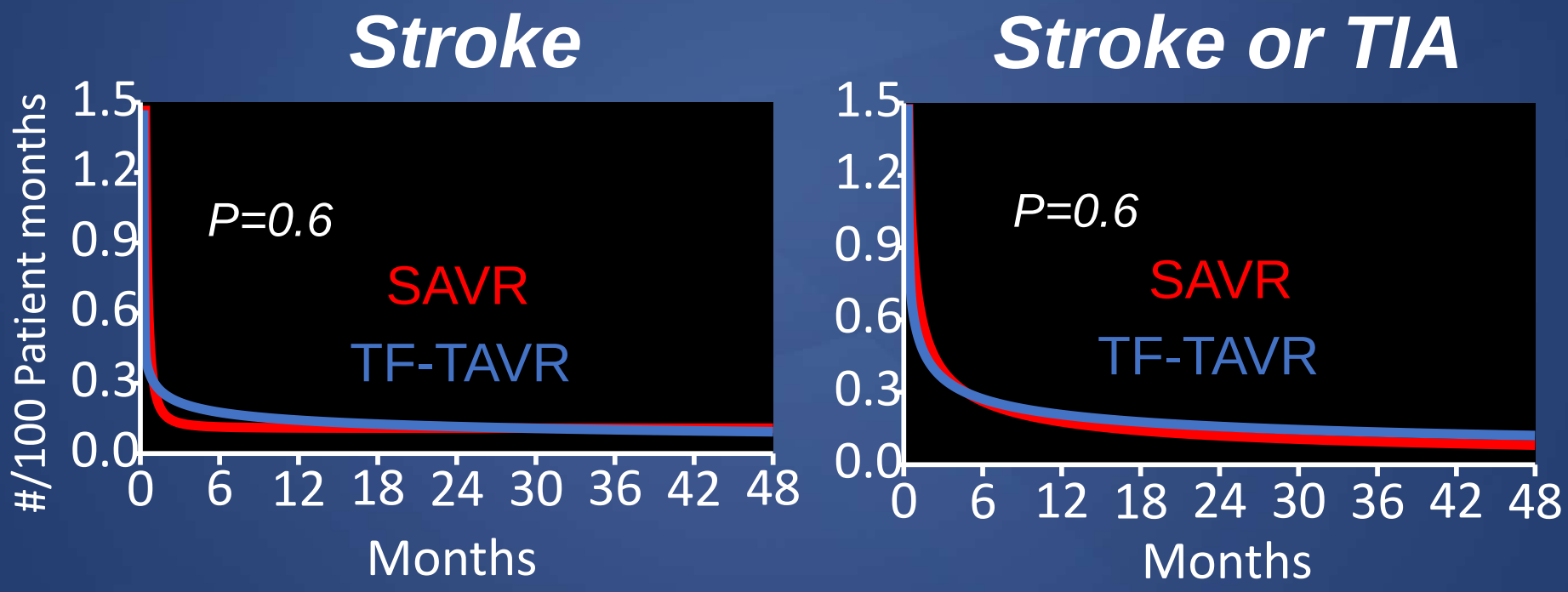
Instantaneous Risk Modeling



Samir R. Kapadia et al, J Am Coll Cardiol. 2018;72:2415–26.

Late Phase Risk (4 Years)

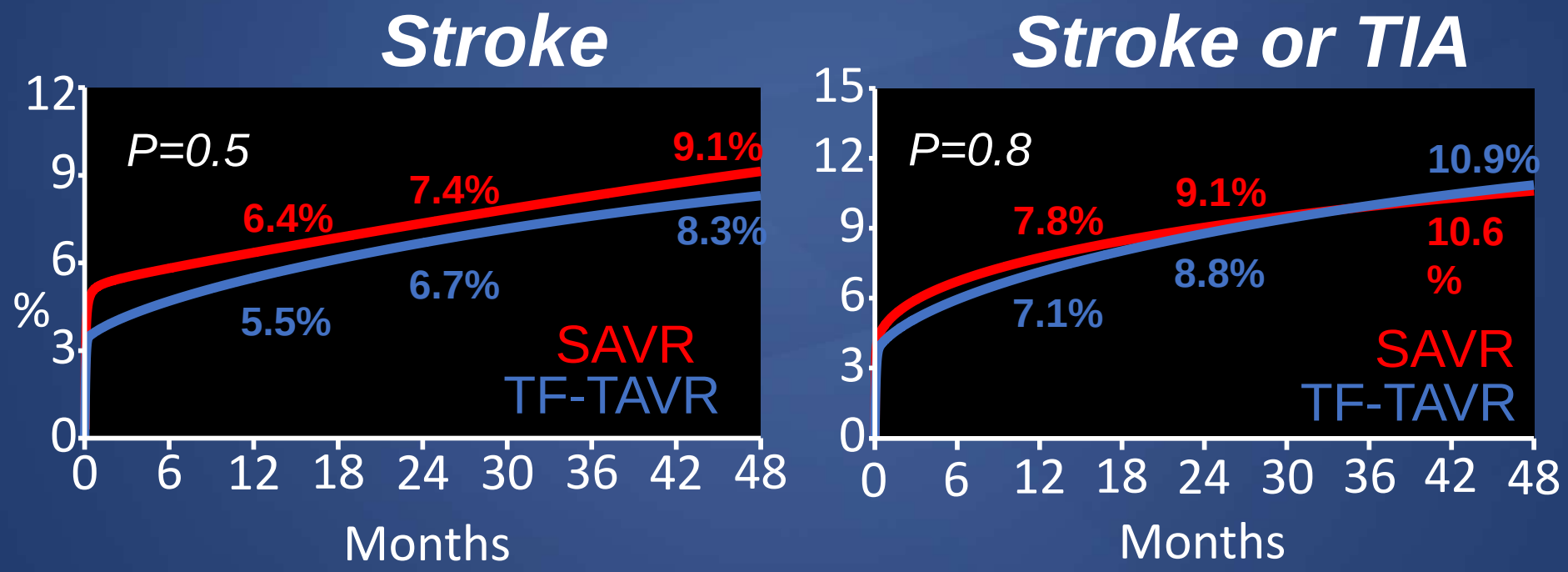
Instantaneous Risk Modeling



Samir R. Kapadia et al, J Am Coll Cardiol. 2018;72:2415–26.

Cumulative Incidence of Events

Adjusted for Competing Risk of Mortality



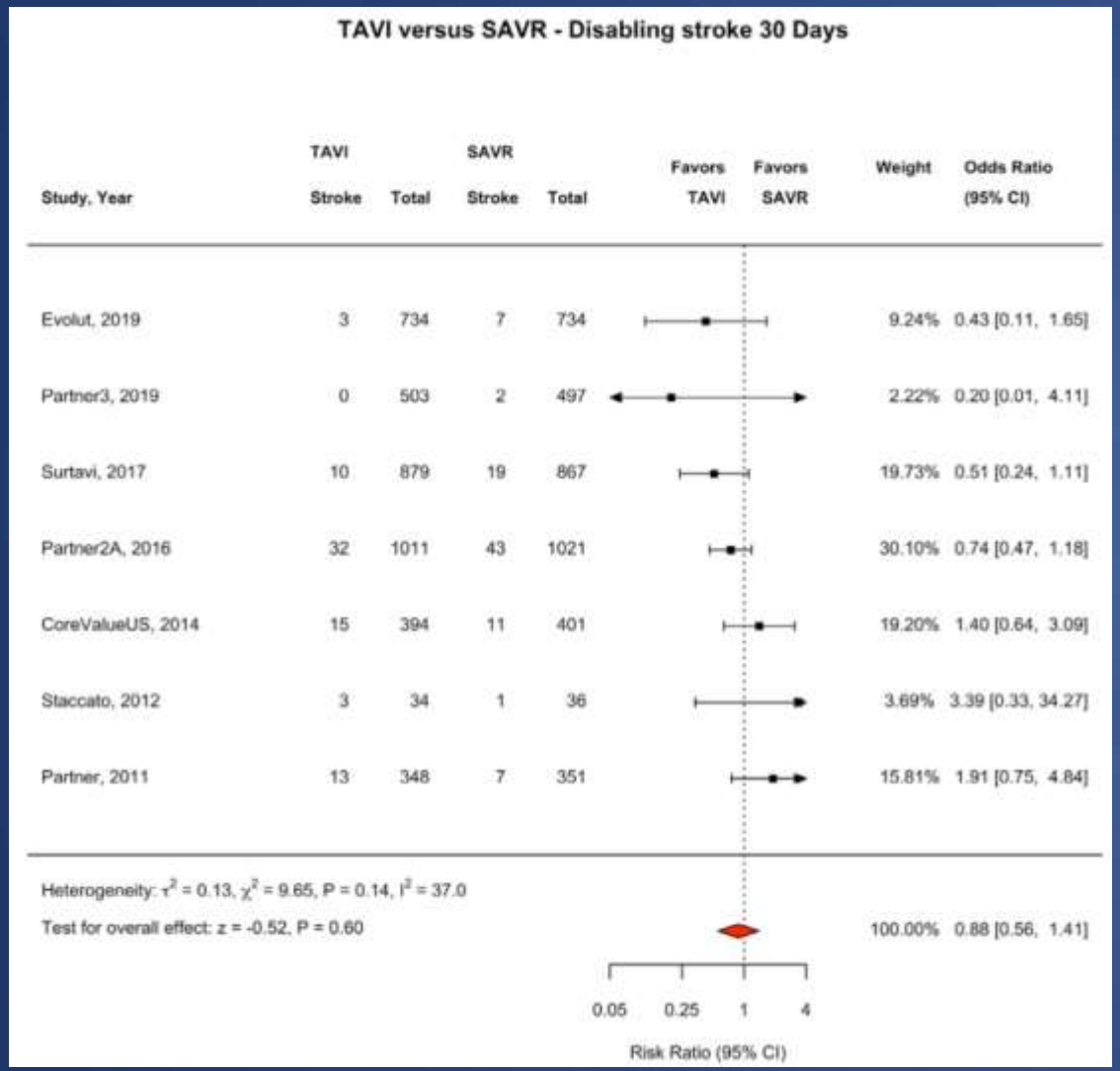
Samir R. Kapadia et al, J Am Coll Cardiol. 2018;72:2415–26.

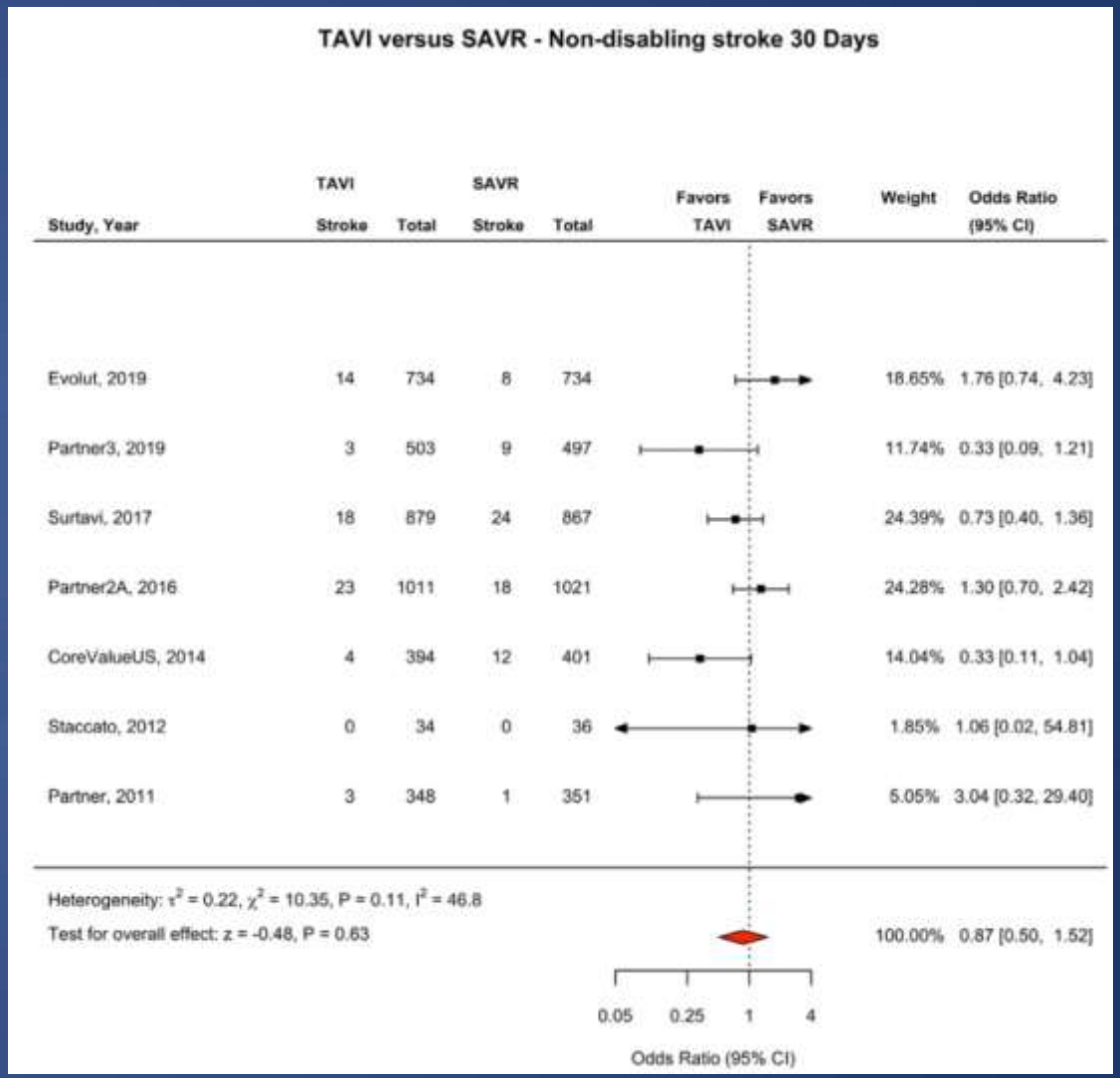
Stroke Severity in TAVR vs SAVR

: A Systematic Review and Meta-Analysis

Padraig Synnott MB et al, Journal of Stroke and Cerebrovascular Diseases, Vol. 30, No. 9 (September), 2021:105927

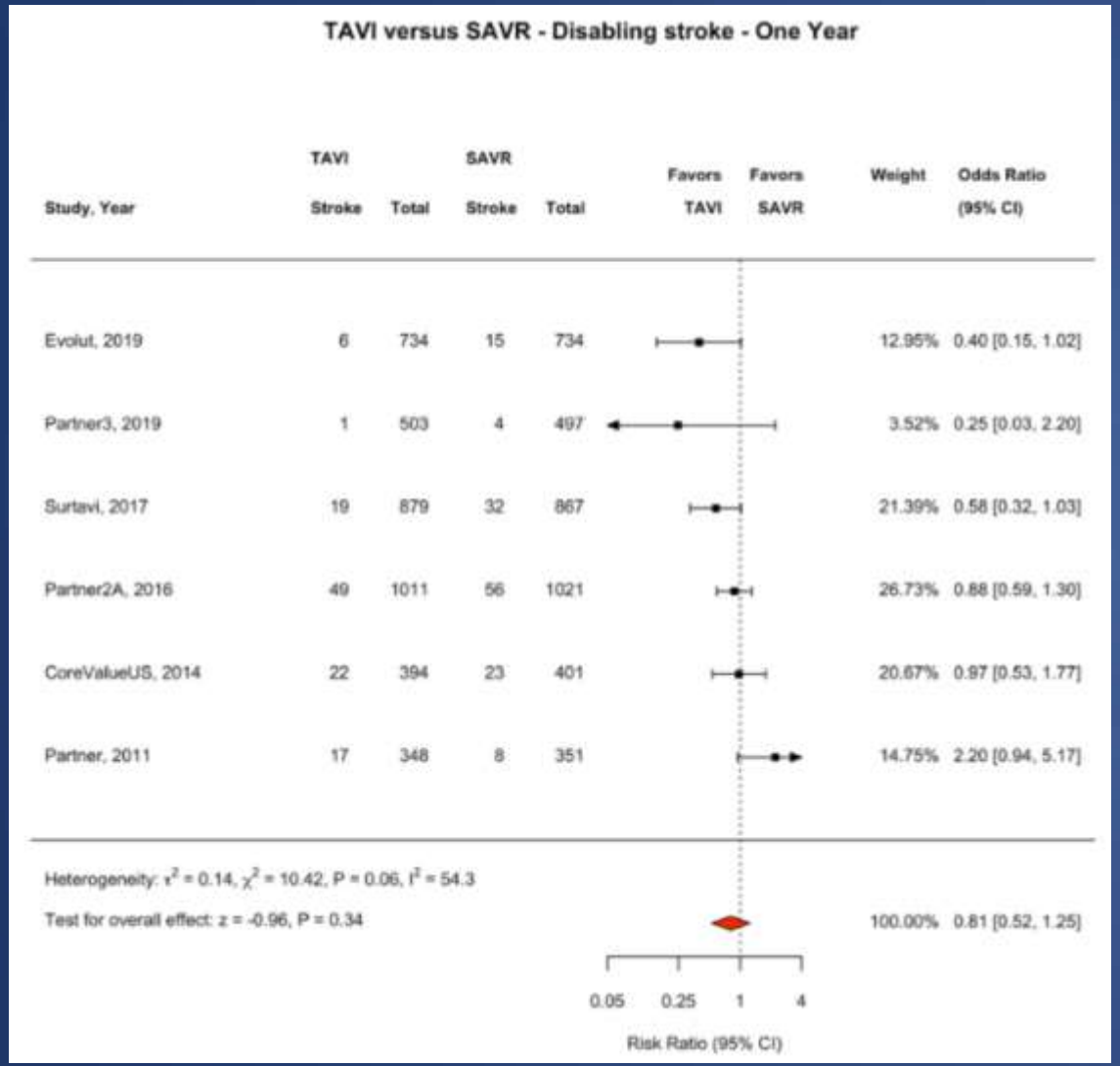
Disabling and Non-disabling stroke 30 Days

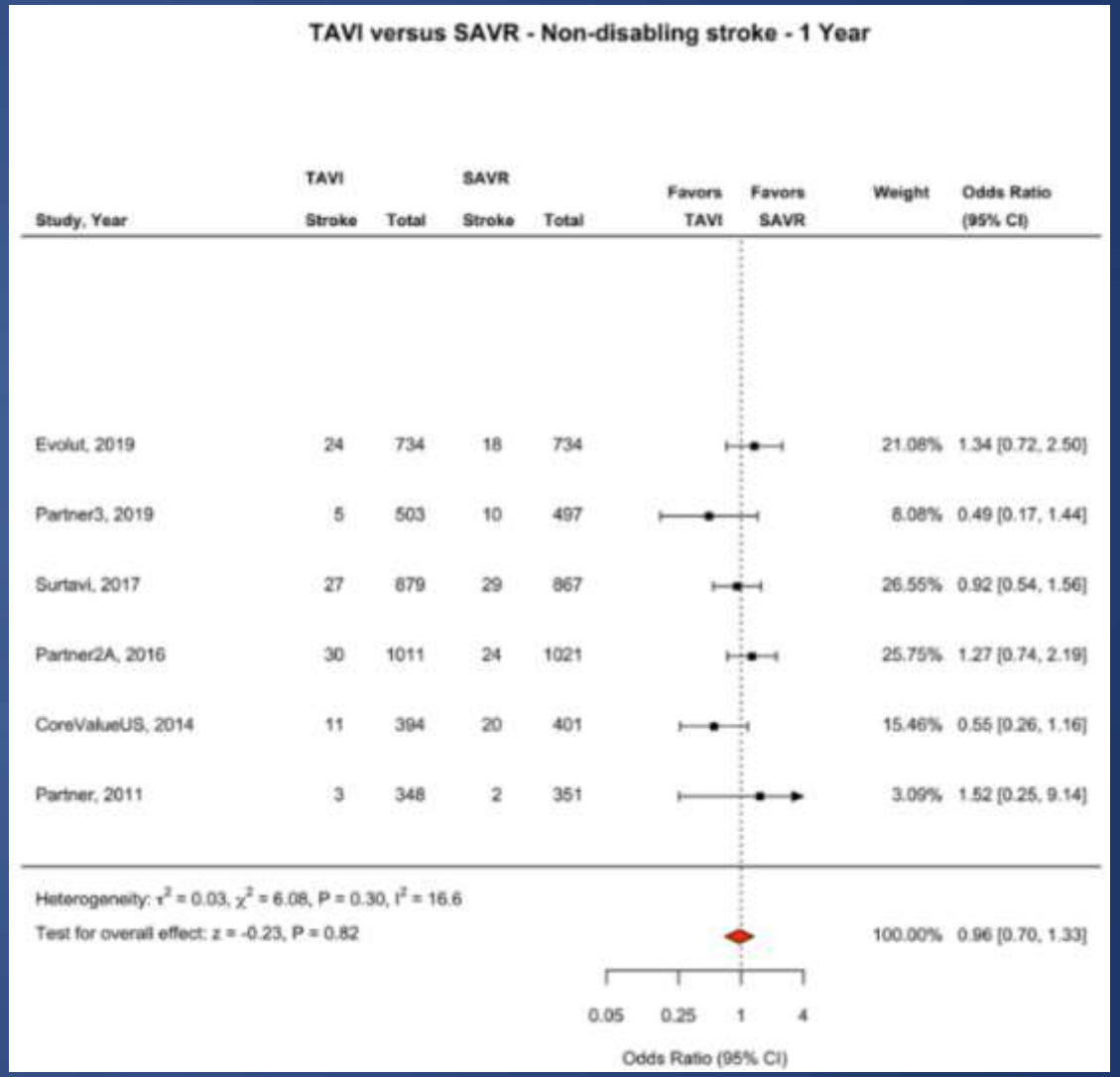




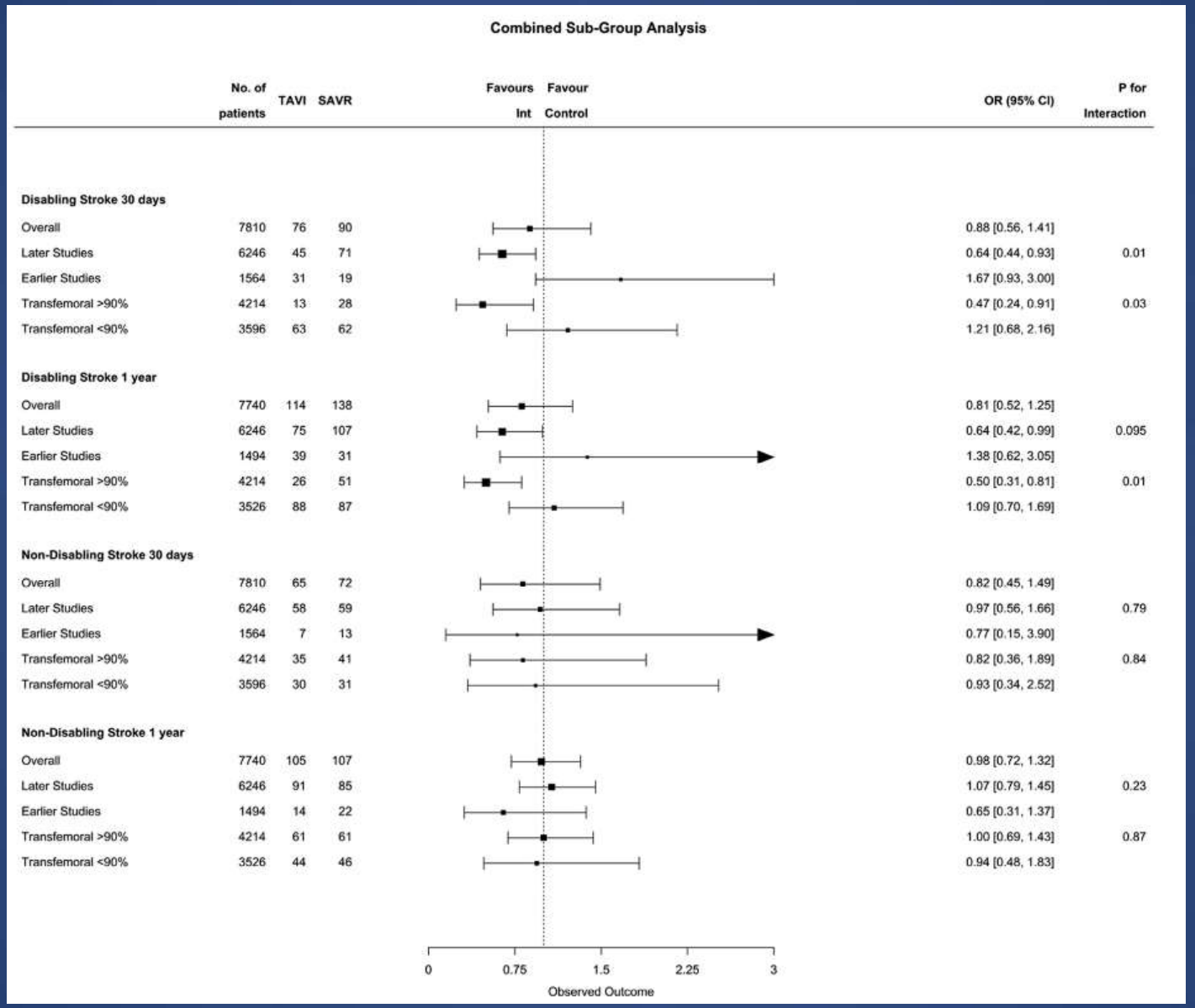
Padraig Synnott MB et al, Journal of Stroke and Cerebrovascular Diseases, Vol. 30, No. 9 (September), 2021:105927

Disabling and Non-disabling stroke 1 Year





Padraig Synnott MB et al, Journal of Stroke and Cerebrovascular Diseases, Vol. 30, No. 9 (September), 2021:105927



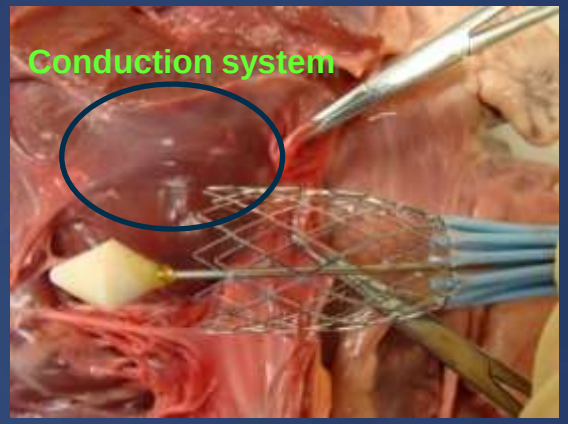
Padraig Synnott MB et al, Journal of Stroke and Cerebrovascular Diseases, Vol. 30, No. 9 (September), 2021:105927

Conduction Disturbance

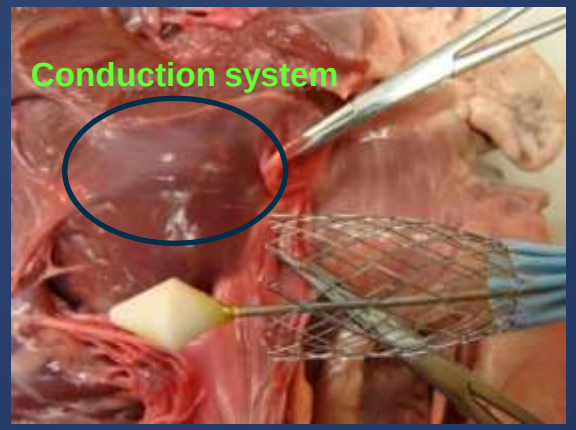
Type

- Left Bundle Branch Block
- AV Conduction Disturbances
- Complete Heart Block

Depth of Implantation

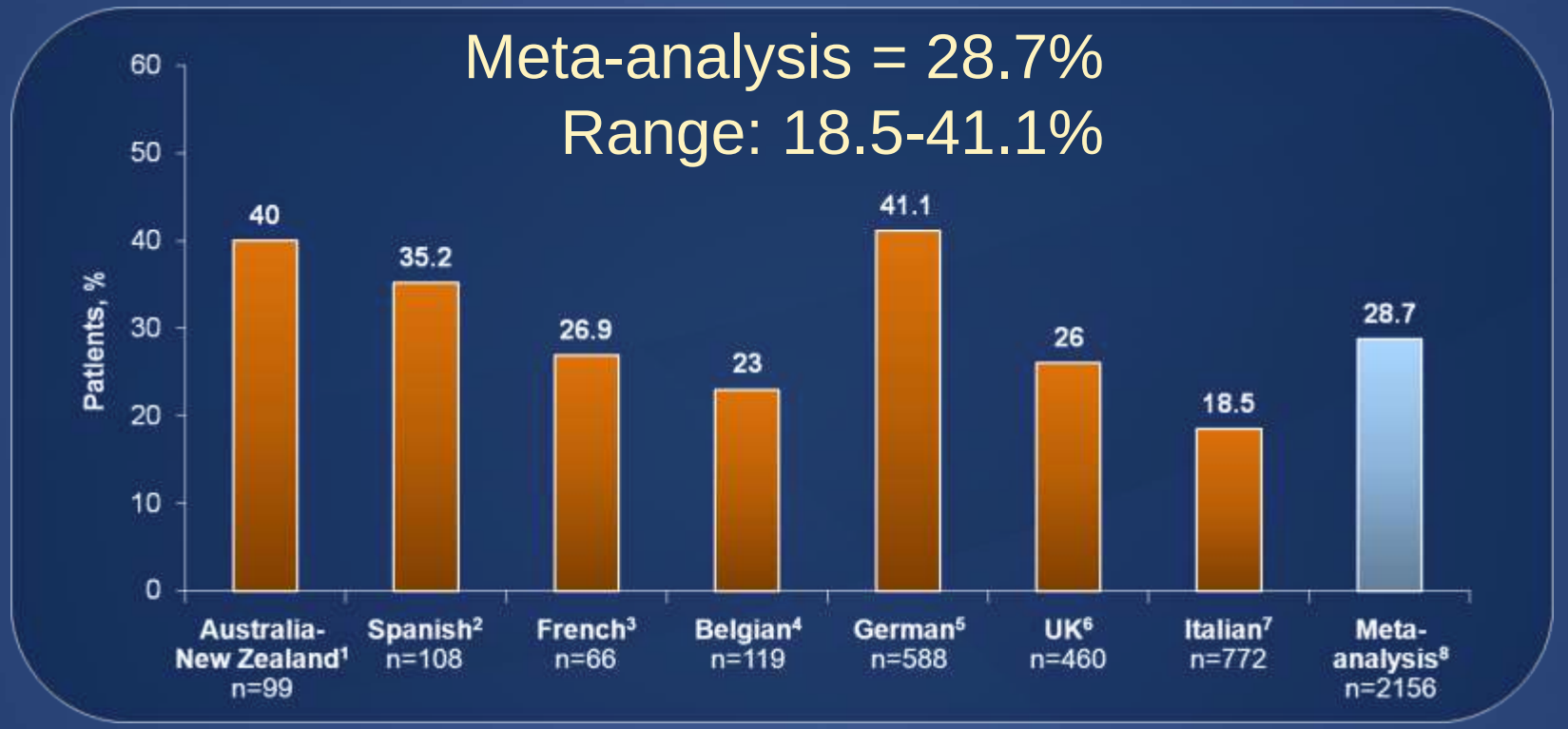


15mm -
past annulus



5mm -
past annulus

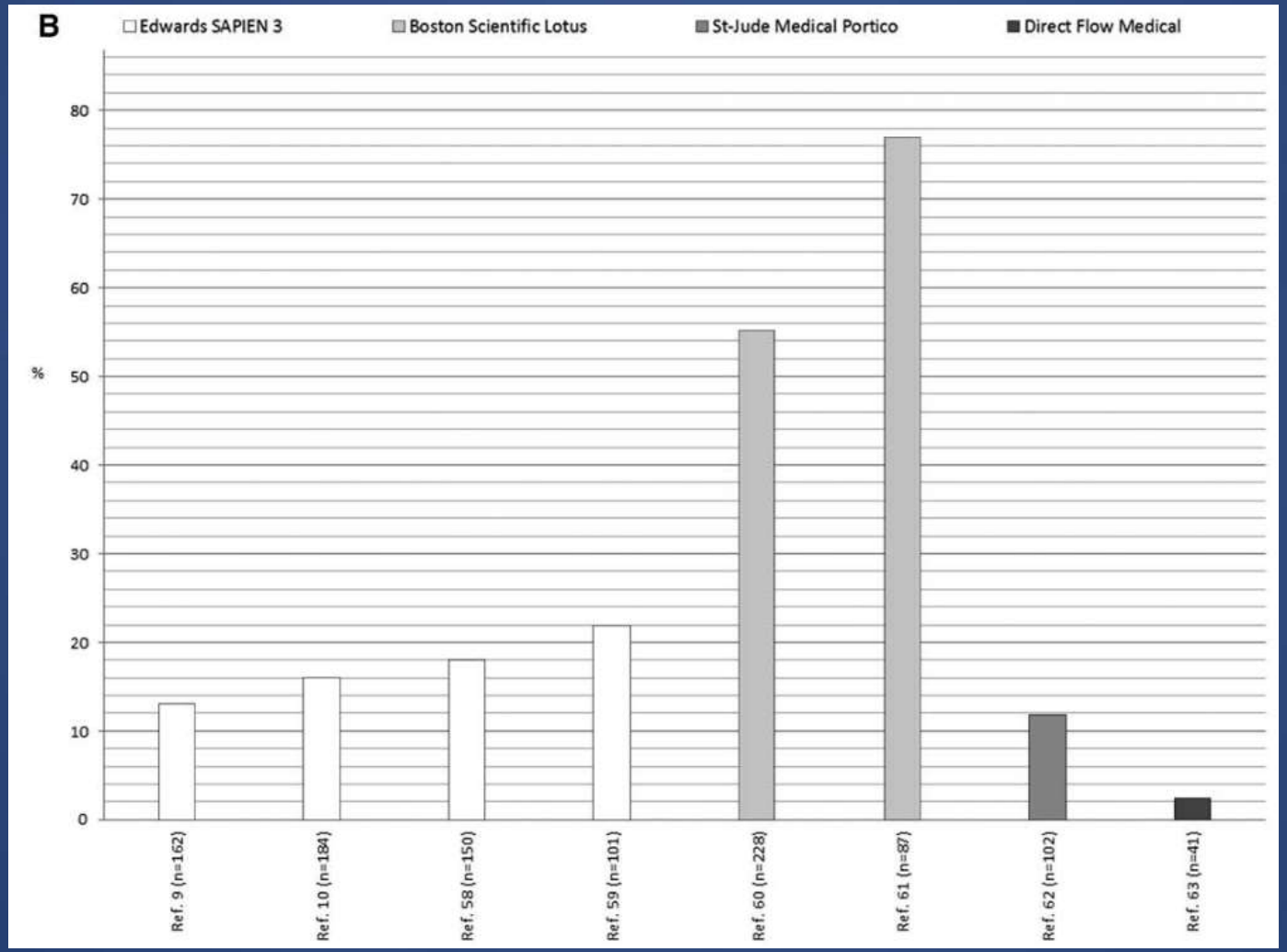
CoreValve Meta-analysis : PPM



1. Meredith IT. The Australia-New Zealand Medtronic CoreValve® Registry: outcomes in inoperable and high risk AS patients. Presented at: TCT. 2010.
2. Avanzas P, et al. *Rev Esp Cardiol*. 2010;63:141-148.
3. Eltchaninoff H. French Registry. TAVI facts, figures and national registries. Presented at: EuroPCR; May 25-28, 2010; Paris, France.
4. Bosmans J. Belgian Registry. TAVI facts, figures and national registries. Presented at: EuroPCR; May 25-28, 2010; Paris, France.
5. Zahn R. German Registry. TAVI facts, figures and national registries. Presented at: EuroPCR; May 25-28, 2010; Paris, France.
6. Ludman P. UK Registry. TAVI facts, figures and national registries. Presented at: EuroPCR; May 25-28, 2010; Paris, France.
7. Petronio AS. Italian Registry. TAVI facts, figures and national registries. Presented at: EuroPCR; May 25-28, 2010; Paris, France.
8. Ruiz CE, et al. Weighted meta-analysis of early and late clinical outcomes after CoreValve® – TAVI in seven national registries. Presented at: EuroPCR; May 17-20, 2011; Paris, France. Analysis funded by Medtronic, Inc.

Conduction Disturbance

Incidence of new-onset left bundle-branch block (LBBB)



Vincent Auffret et al, Circulation. 2017;136:1049–1069.

Pacemakker Implantation After Balloon- or Self-Expandable TAVR

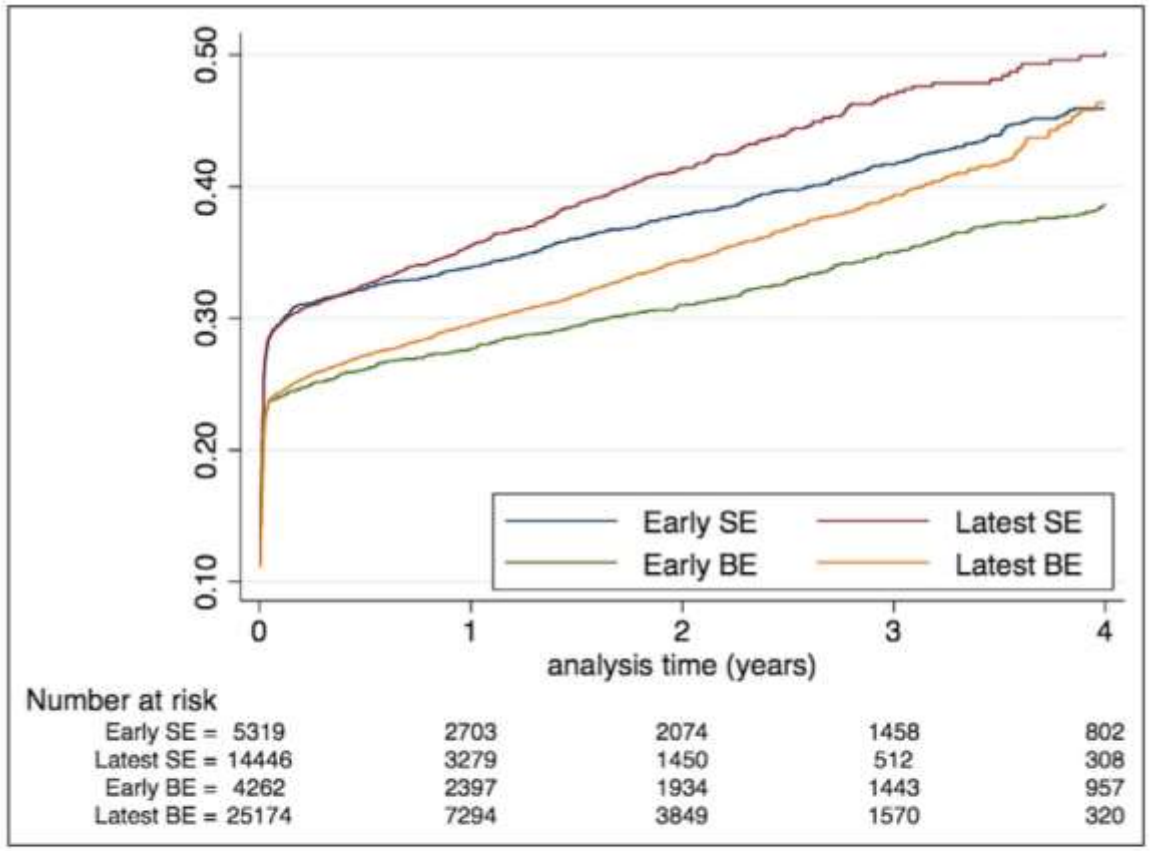


Figure. Incidence of permanent pacemaker implantation in patients treated with TAVR, according to type and generation of device.
BE indicates balloon-expandable; Early BE, Edwards Sapien XT; Early SE, Medtronic Corevalve; Latest BE, Edwards Sapien 3; Latest SE, Medtronic Evolut; SE, self-expandable; and TAVR, transcatheter aortic valve replacement.

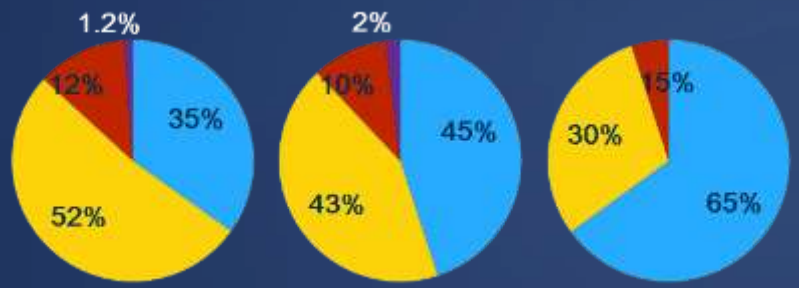
- BE technology was independently associated with lower incidence rates of PPI both at the acute and chronic phases than SE technology.
- Recent generations of TAVR were not independently associated with different rates of PPI than early generations during the overall follow-up.

Arnaud Bisson, et al. J Am Heart Assoc. 2020;9:e015896.

Para-valvular Leak

Incidence of AR

PARTNER Trial



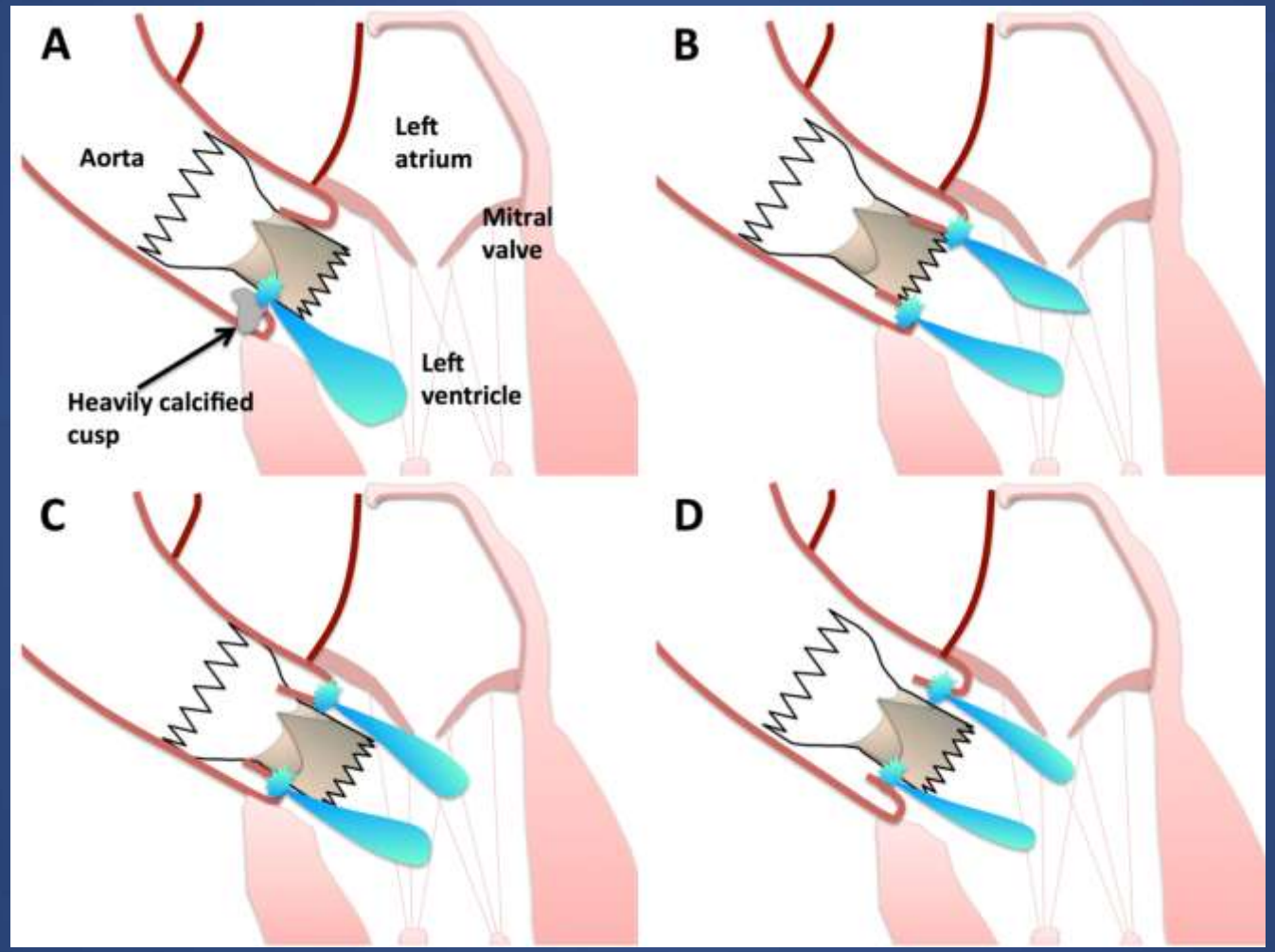
Mechanism

- **Prosthesis expansion**
  - Geometry and degree of apposition
- **Prosthesis apposition**
  - Larger coronal/sagittal annulus diameter
  - Higher calcium score/Heavily calcified commissure
  - More ellipsoid valves
- **Inadequate prosthesis size**
  - Prosthesis-annulus cover index

$$= \frac{100 \times (\text{prosthesis} - \text{TEE annulus}) \text{ diameter}}{\text{prosthesis diameter}}$$

- **Improper prosthesis positioning**

Mechanism of PVL



Sinning JM et al., JACC 2012

Incidence, Predictors, and Outcomes of AR after TAVR

Meta-analysis of 45 studies involving 12,926 patients treated with CoreValve (n = 5,261) or Edwards valves (n = 7,279).

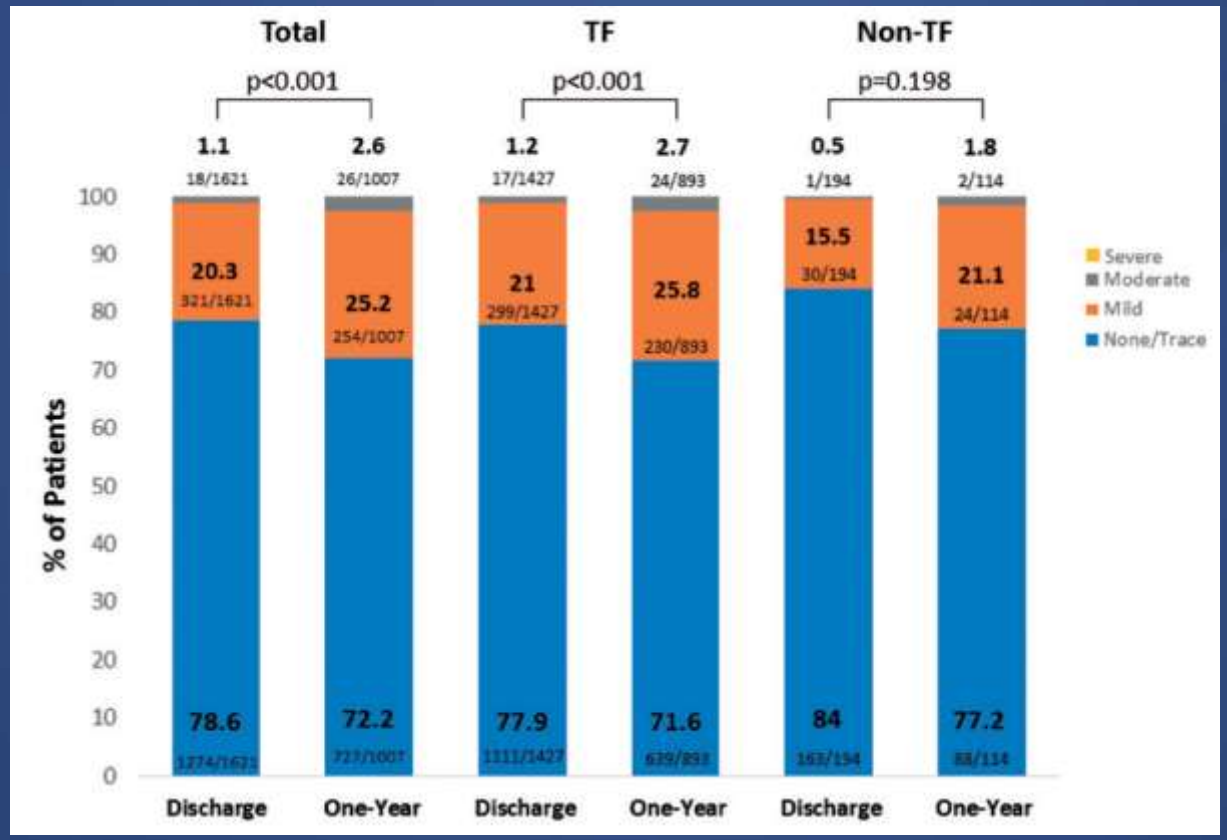
- Incidence of moderate/severe AR was 11.7%
- More common with CoreValve than with Edwards(16.0% vs. 9.1%; *P* = 0.005)
- Moderate/severe AR increased mortality at 30 days (OR 2.95; 95% CI 1.73-5.02) and 1 year (HR 2.27; 95% CI 1.84-2.81)
- Even mild AR was linked to mortality in some studies
- Predictors of moderate/severe AR were valve undersizing, aortic valve calcification, and implantation depth

Implications: Aortic regurgitation is fairly common after TAVR and appears to increase mortality even when mild.

Athappan G, et al. J Am Coll Cardiol. 2013;61:1585-1595.

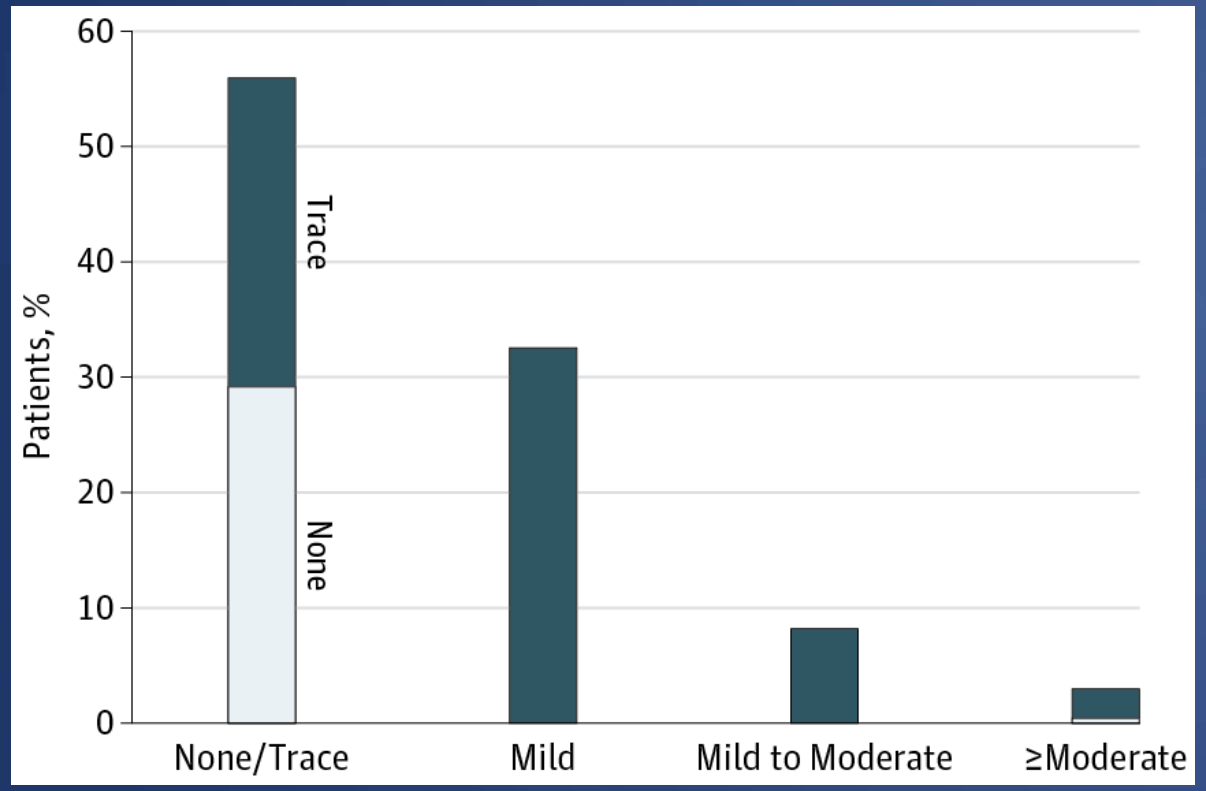
SOURCE 3 : 1yr outcome

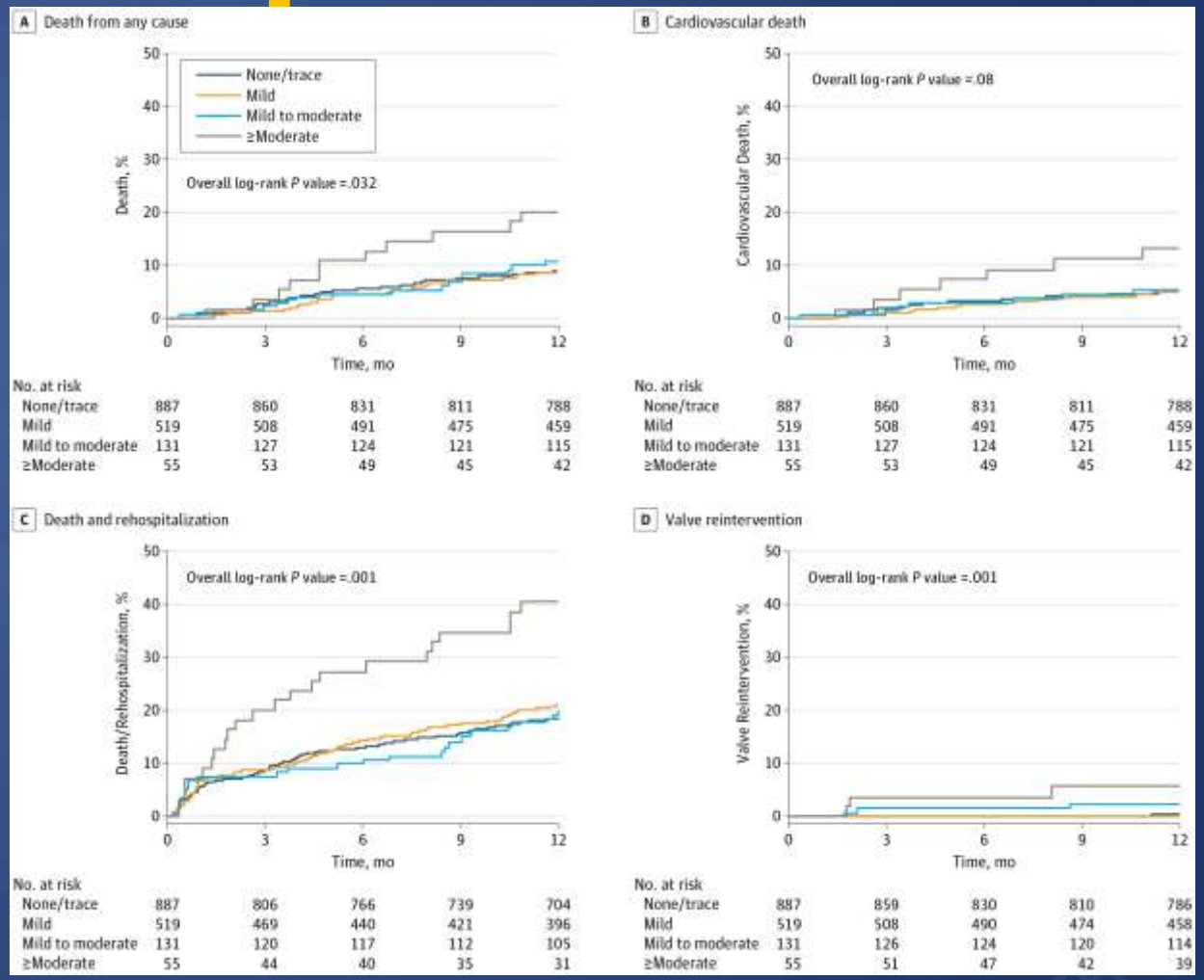
PVL (mod-severe) for 1yr mortality : HR 0.09 (0.00, NA), p = 0.97



Wendler O et al. EHJ 2017 Jun. Epub ahead of print

Association of PVL with 1-year Outcomes After TAVR with the Sapien 3 valve





Philippe Pibarot, DVM et al. JAMA Cardiol. 2017;2(11):1208-1216

Vascular Complication

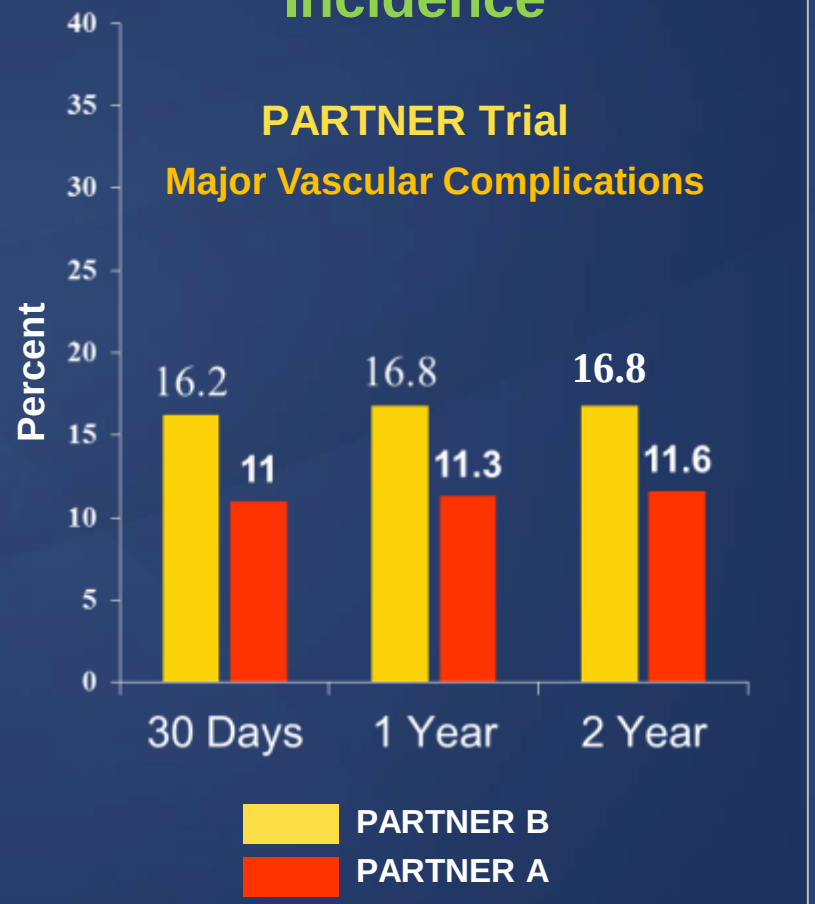
Type

- Posterior wall puncture / High stick
- Dissection
- Perforation
- Closure device failure
- Foreign body embolization

Potential Risk Factors

- Operator related : poor screening, Aggressive manipulation, Not prepared for complication
- Patient related : Vessel size, Tortuousity, Calcification, Atherosclerosis
- Device related : Sheat size, Delivery system, Wire, Pacemaker, BAV balloon, Closure device

Incidence



Coronary Obstruction

Possible Causes

- LMT ostium close to the annulus
- Bulky calcific deposit on left cusp
- Long left location of the LMT ostium
- Narrow aortic root with shallow sinuses of valsalva
- Oversized valve
- Pliable, minimally calcific left leaflet
- Proximal septal bulge
- Aortic atherosclerosis near to the ostium
- Embolism
- Improper valve position

Risk of Coronary Obstruction

Multifactorial

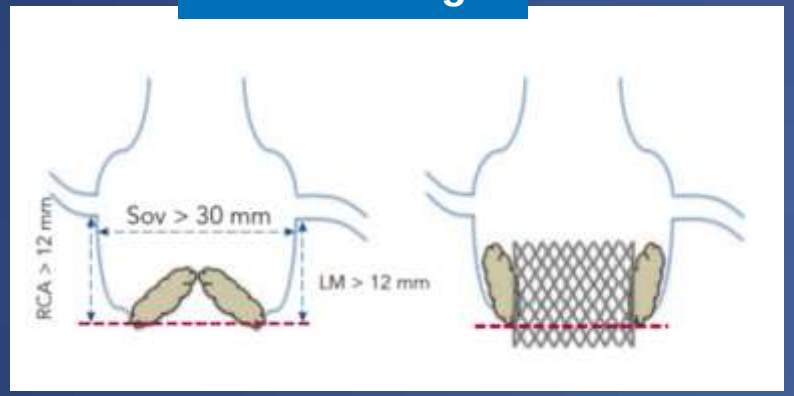
- Women
- Low Coronary Height (<10mm to <12mm)
- Shallow Sinus of Valsalva (<30mm)
- Long Leaflet
- Left Coronary Artery
- Bulky Calcification
- Valve Implantation Height
- Device (Balloon Expandable)

Yamamoto M, et al. Int J Cardiol. 2016 May 4;217:58-63

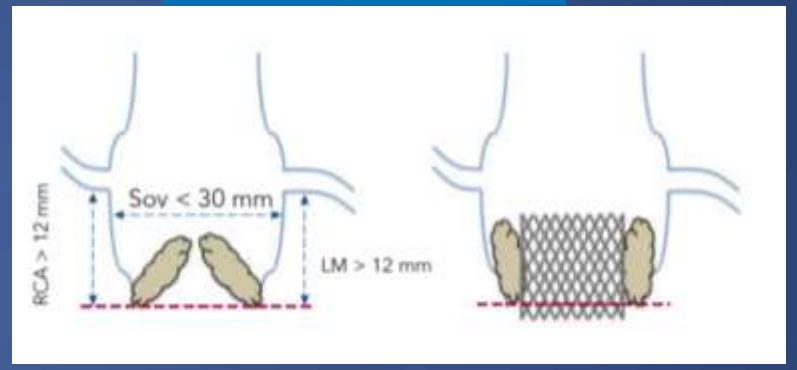
Riberiro HB, et al. J Am Coll Cardiol. 2013 Oct 22;62(17):1552-62

Aortic Root Scenarios

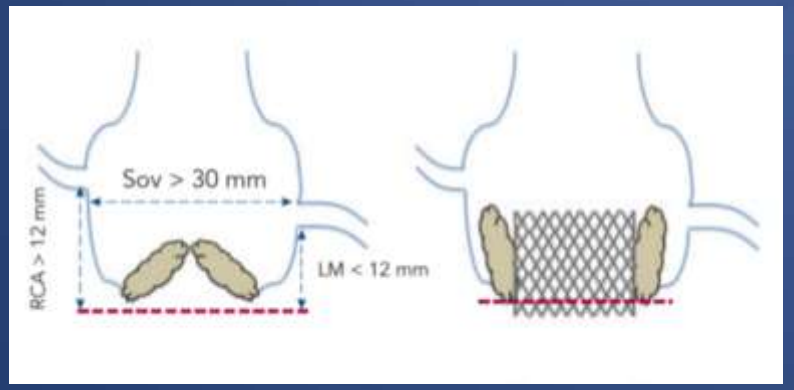
Wide and High



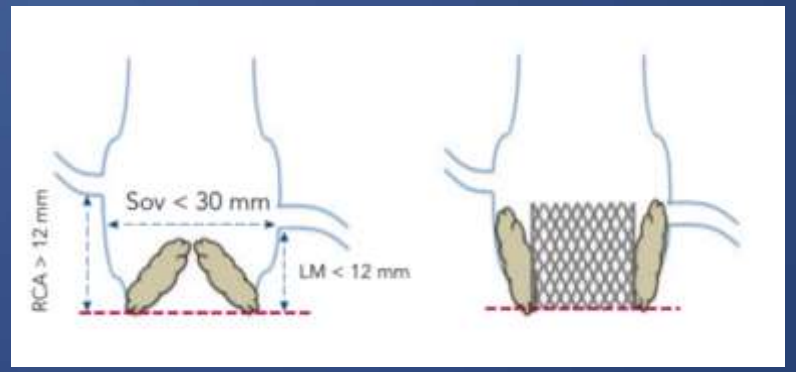
Shallow and High



Wide and Low



Shallow and Low



Interventional Cardiology Review, 2015;10(2):94–7

Infective Endocarditis

- **Incidence** <1%

(similar to that of endocarditis following surgical AVR)

- **Microbiology**

Coagulase-negative Staphlococci (25%)

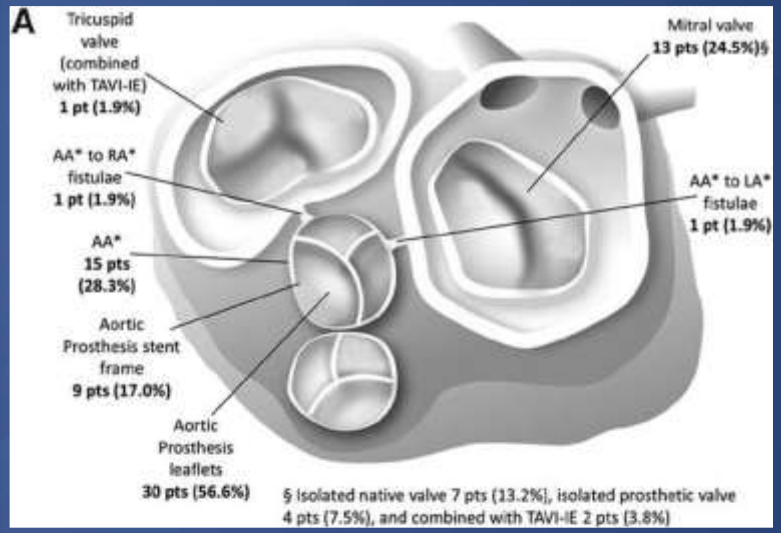
S. aureus (21%), Enterococci (21%)

S. viridans (6%), Unknown (4%)

- **Management and outcomes**

Valve intervention (11%), surgical valve implantation (8%), Valve-in-valve (4%), In-hospital death (47%), Cumulative death (72%)

Location of Infective Endocarditis



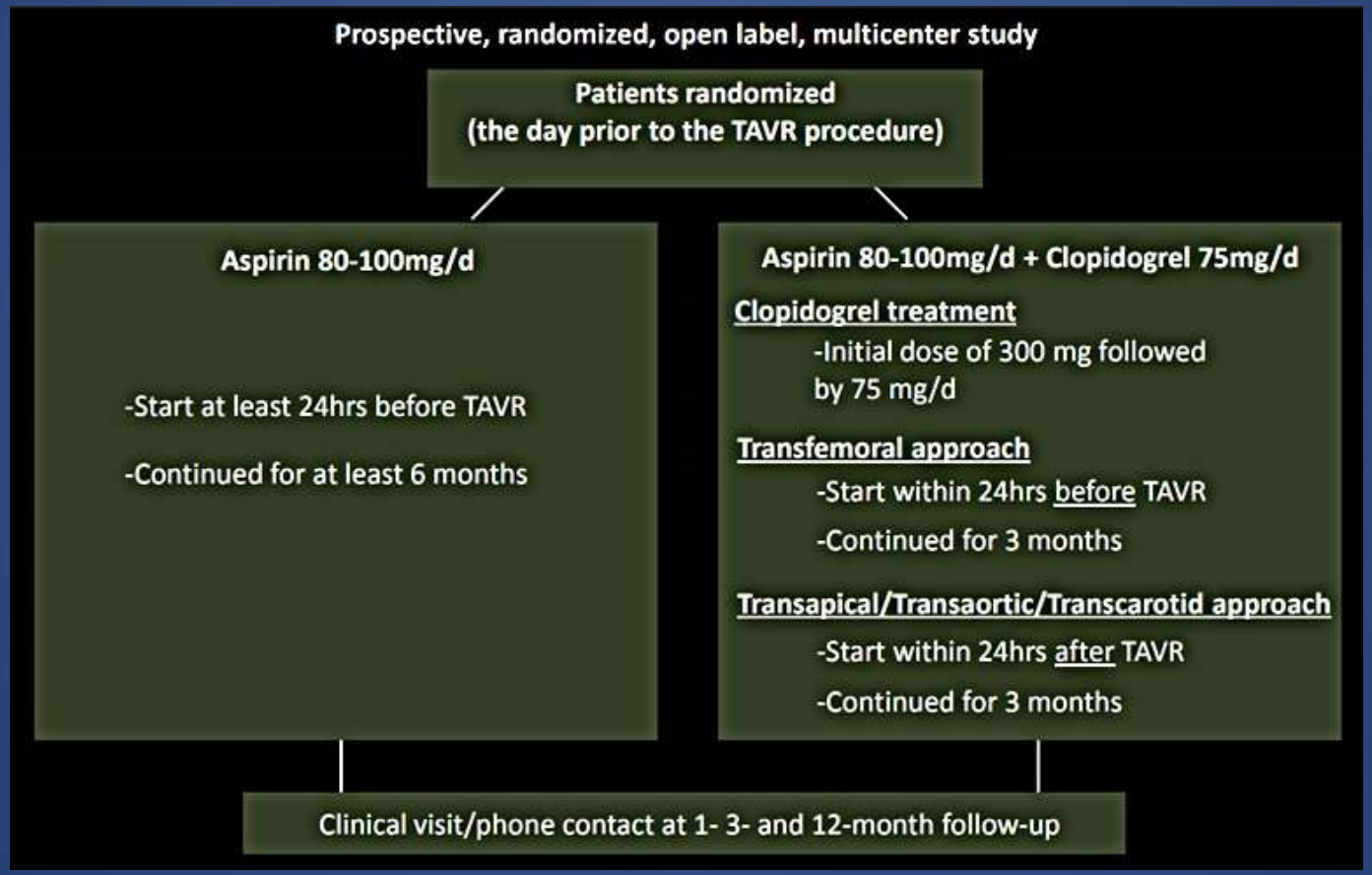
*AA; Ascending Aorta
LA; Left Atrium
RA; Right Atrium

Amat-Santos et al., Circulation . 2015;131:1566-1574

Antithrombotics after TAVR

ARTE Trial

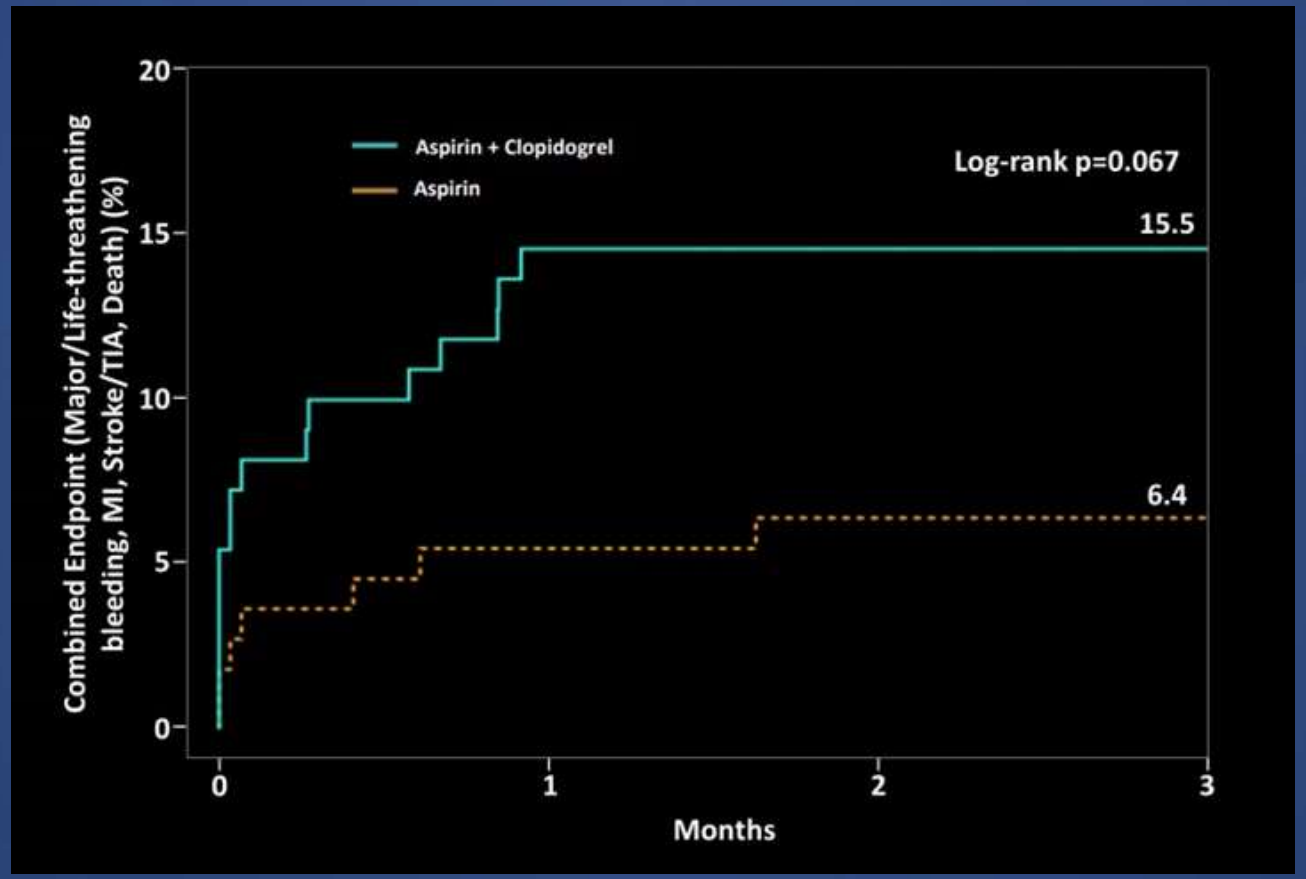
Aspirin alone vs. Aspirin + clopidogrel



Josep Rodes-Cabau et al. 2017 EuroPCR

ARTE Trial

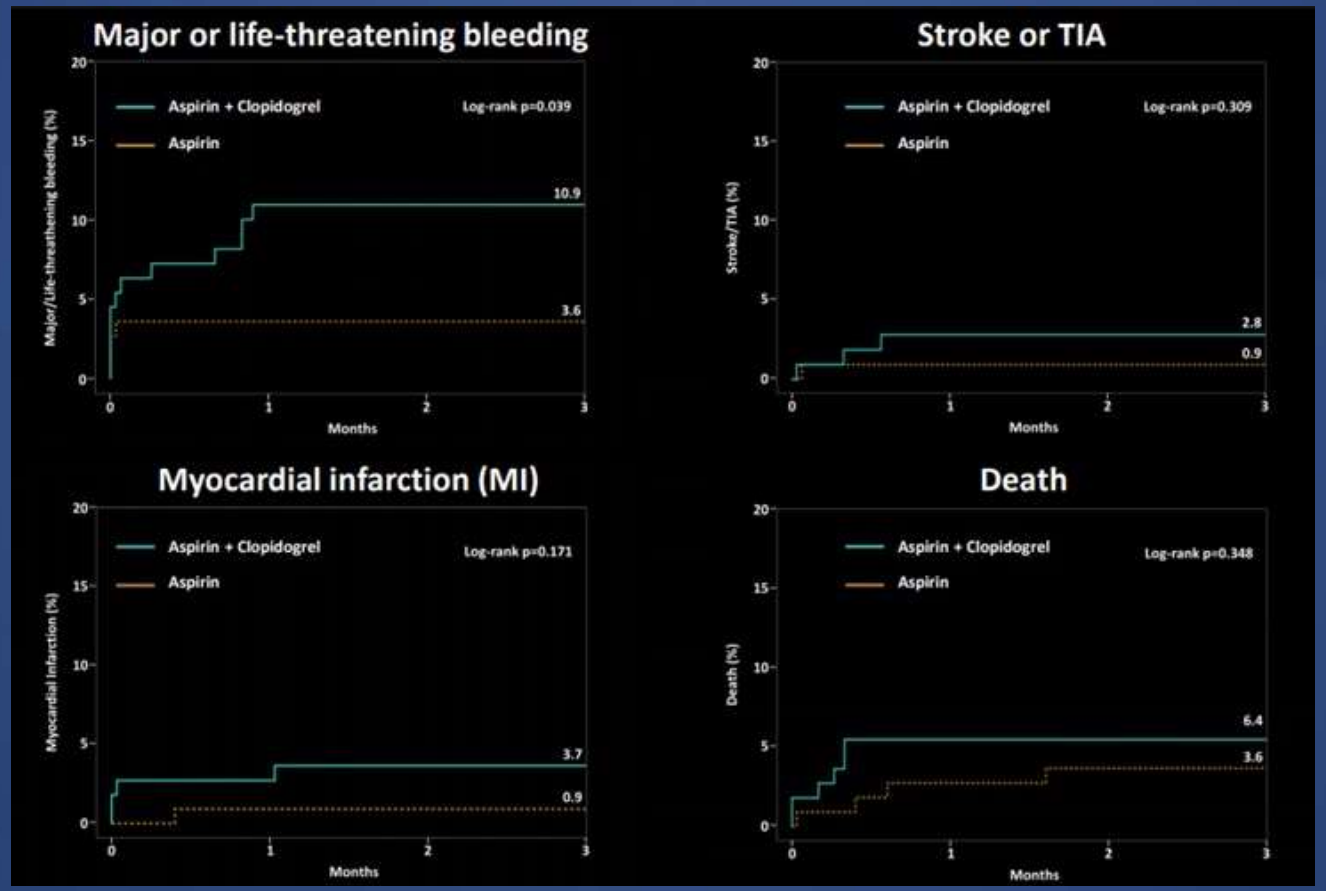
Aspirin alone vs. Aspirin + clopidogrel



Josep Rodes-Cabau et al. 2017 EuroPCR

ARTE Trial

Aspirin alone vs. Aspirin + clopidogrel



Josep Rodes-Cabau et al. 2017 EuroPCR

POPular TAVI Trial

Aspirin alone vs. Aspirin + clopidogrel

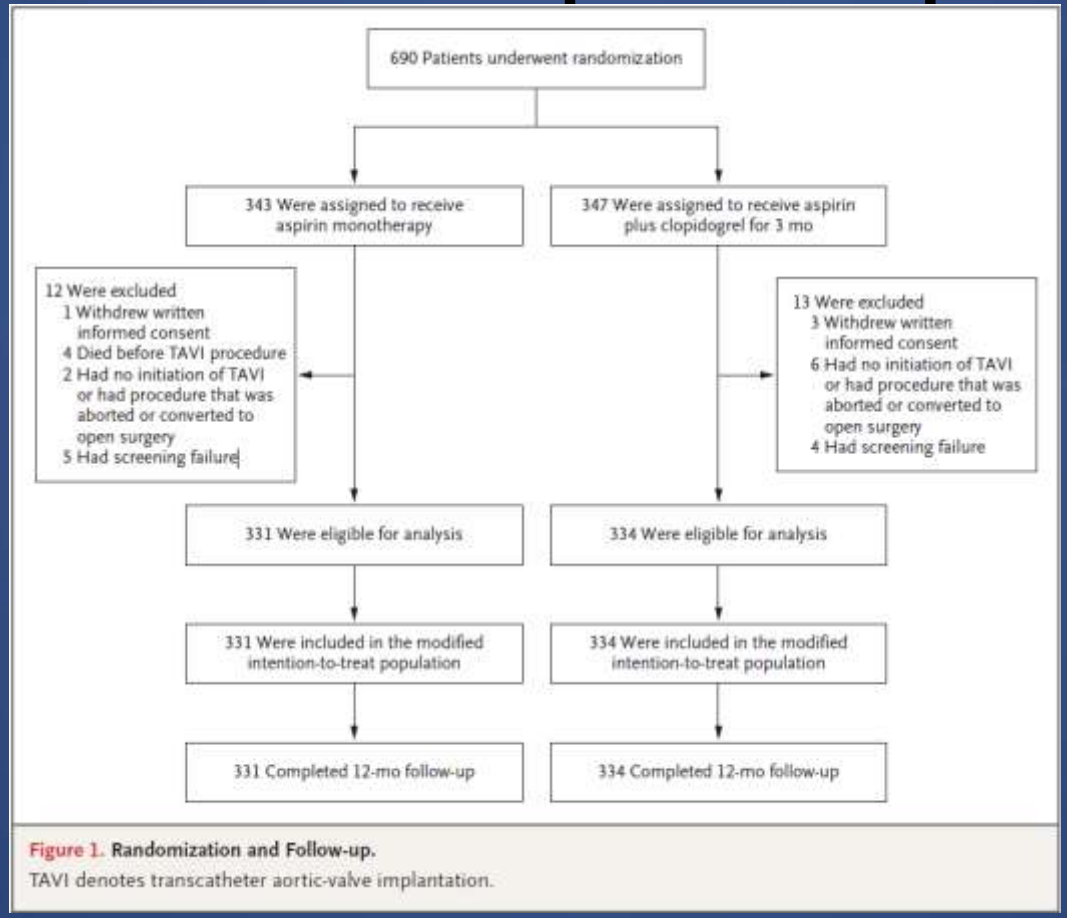
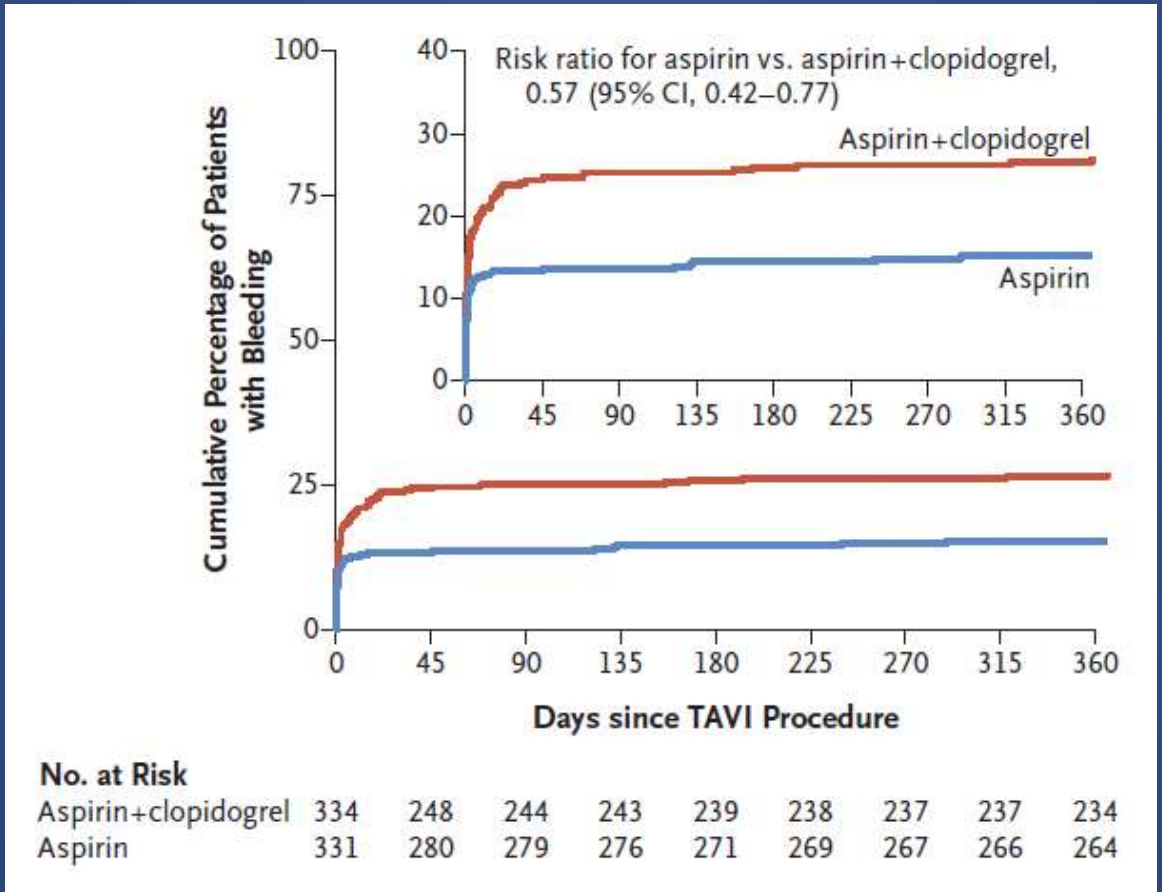


Figure 1. Randomization and Follow-up.
TAVI denotes transcatheter aortic-valve implantation.

J. Brouwer et al. 2020 N Engl J Med. 2020;383:1447-57

POPular TAVI Trial

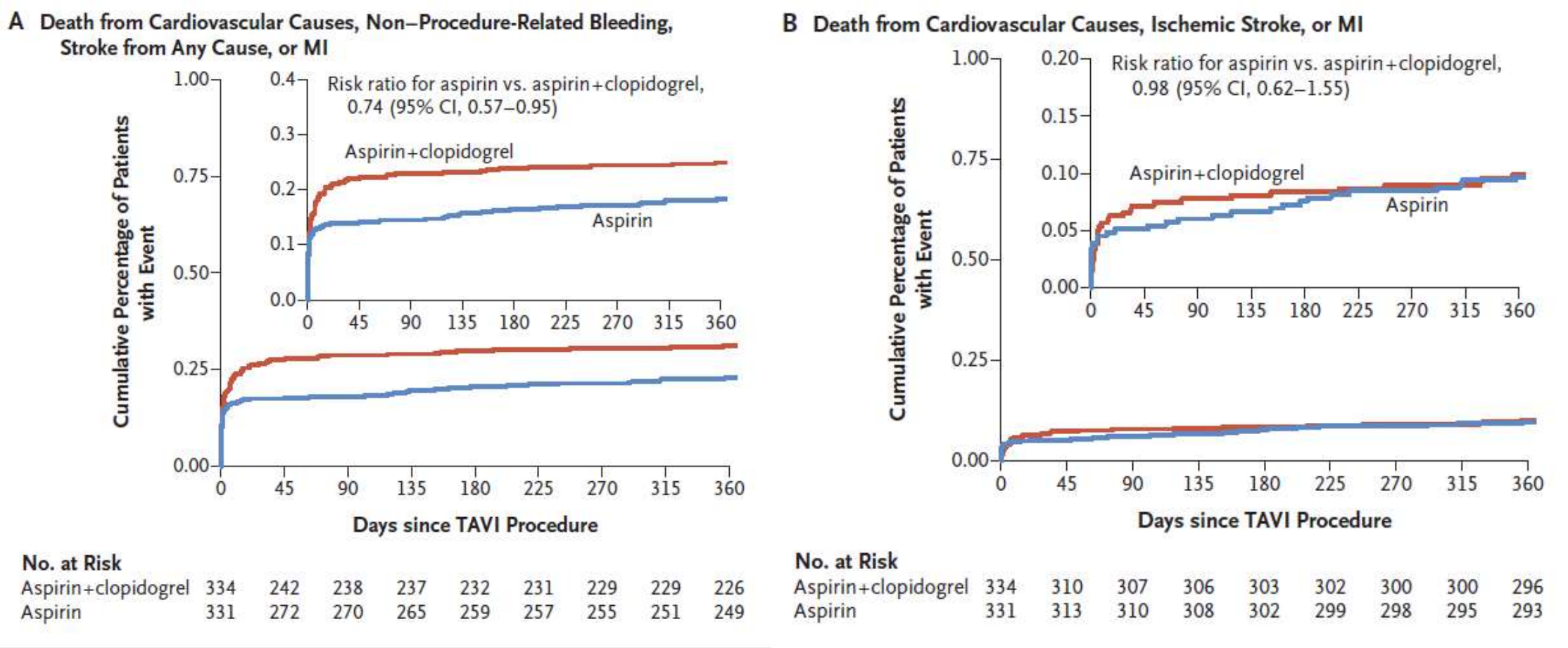
Aspirin alone vs. Aspirin + clopidogrel



J. Brouwer et al. 2020 N Engl J Med. 2020;383:1447-57

POPular TAVI Trial

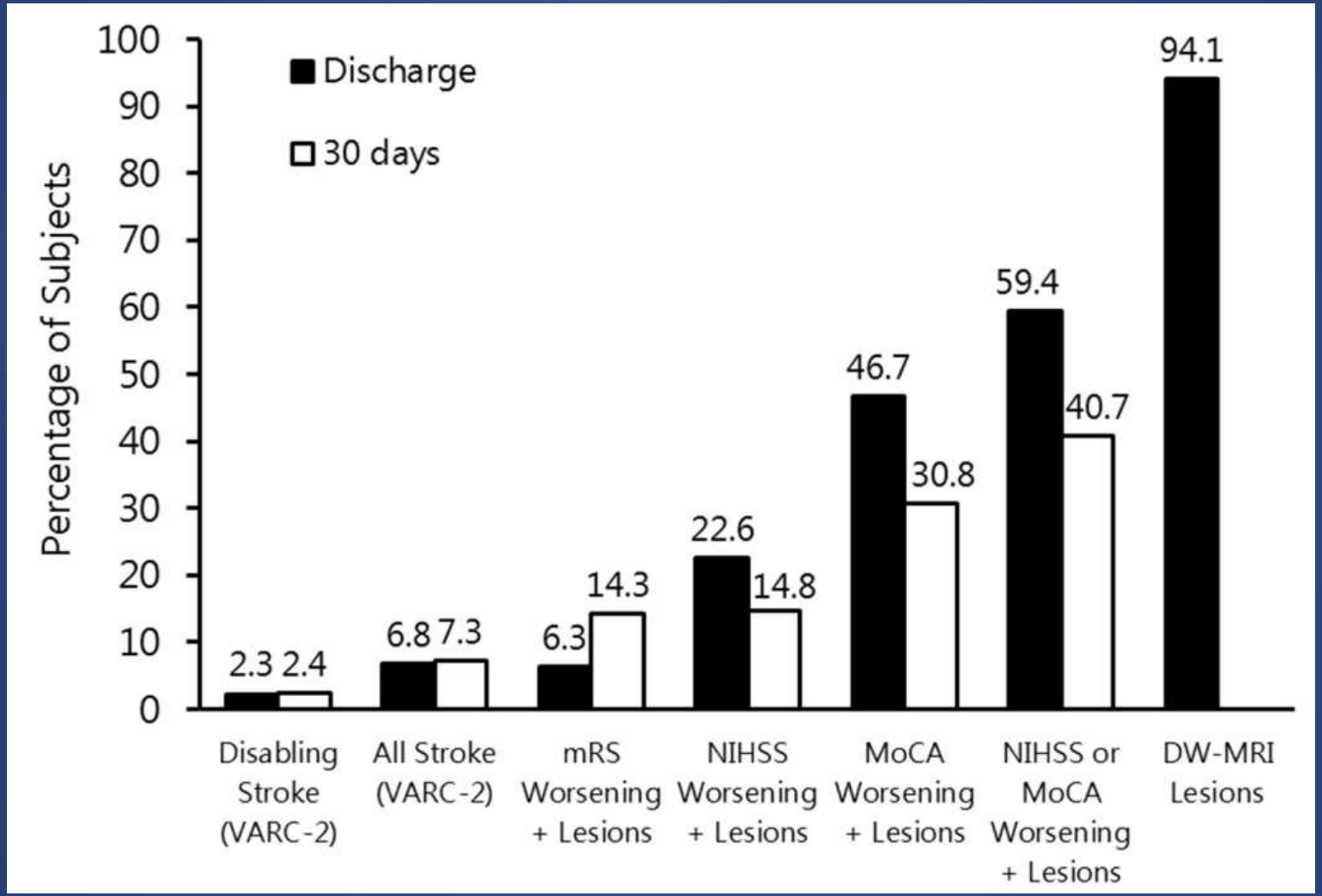
Aspirin alone vs. Aspirin + clopidogrel



J. Brouwer et al. 2020 N Engl J Med. 2020;383:1447-57

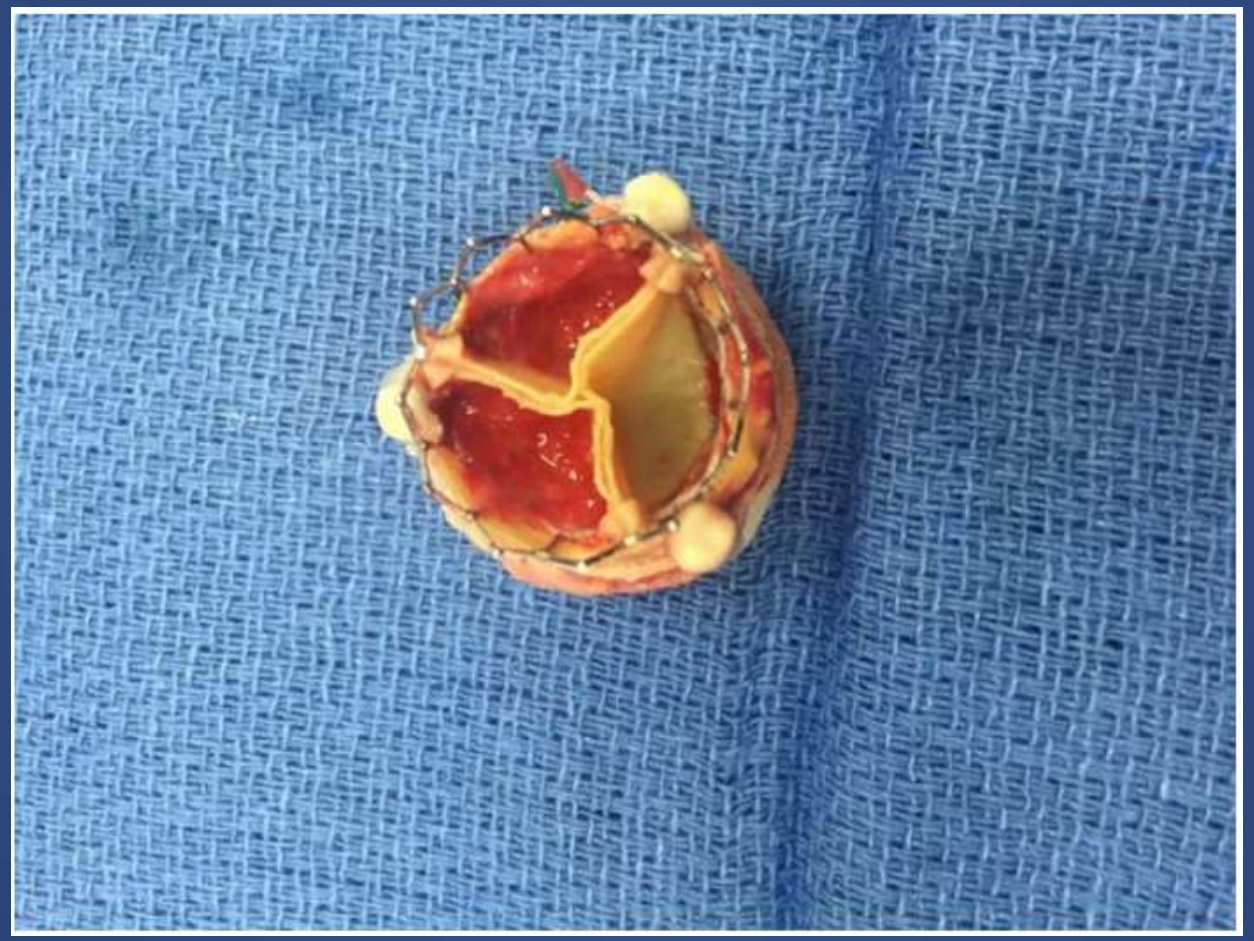
Leaflet Thrombosis

Neurological injury after TAVR From Neuro-TAVI trial



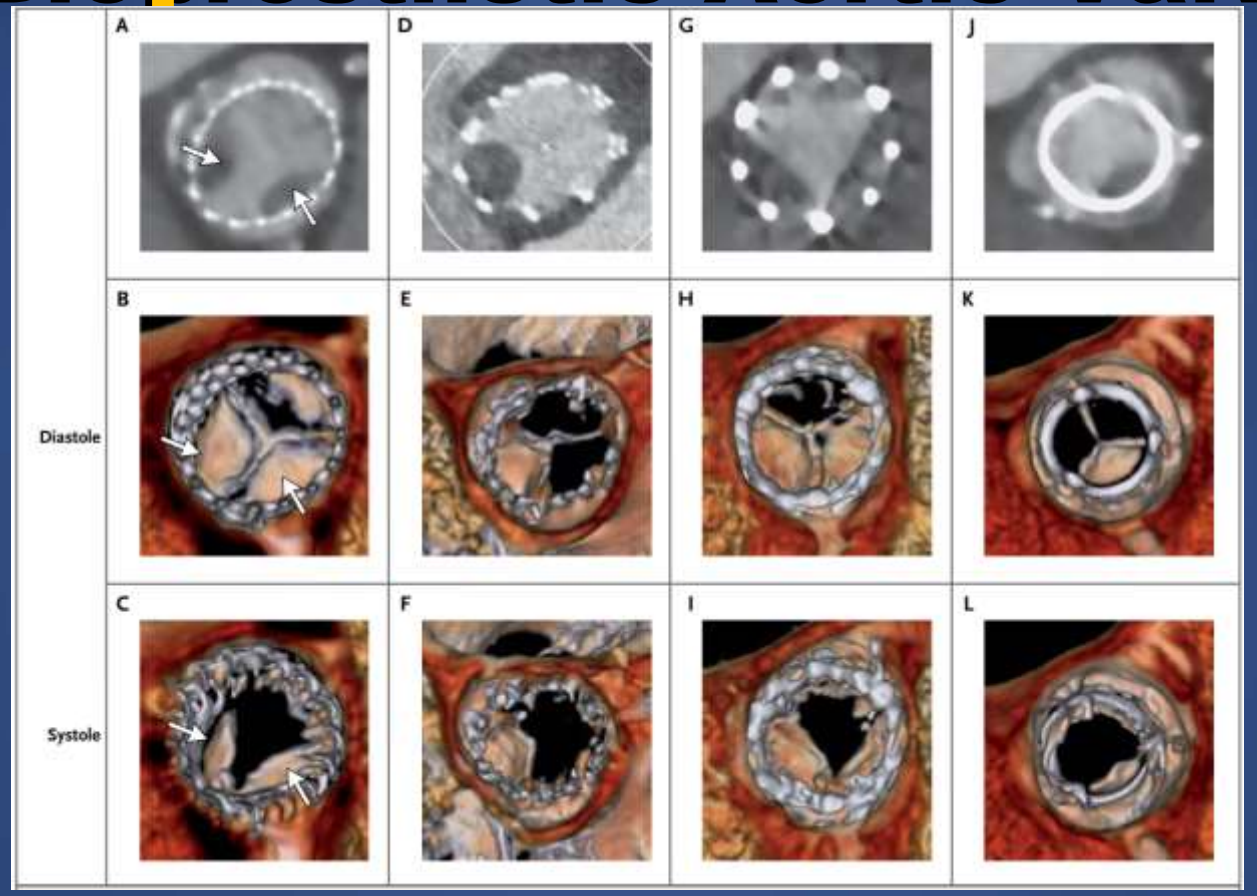
Alexandra J. Lansky and John K. Forrest et al. Am J Cardiol 2016.

Excised TAVR with thrombosis



David R. Holmes and Michael J. Mack. Circulation 2017.

Subclinical Leaflet Thrombosis In Bioprosthetic Aortic Valves



Implications: Reduced aortic-valve leaflet motion was shown in patients with bioprosthetic aortic valves and was easily detected noninvasively by four- dimensional, volume-rendered CT.

R.R Makkar and L. Sondergaard et al. NEJM 2015

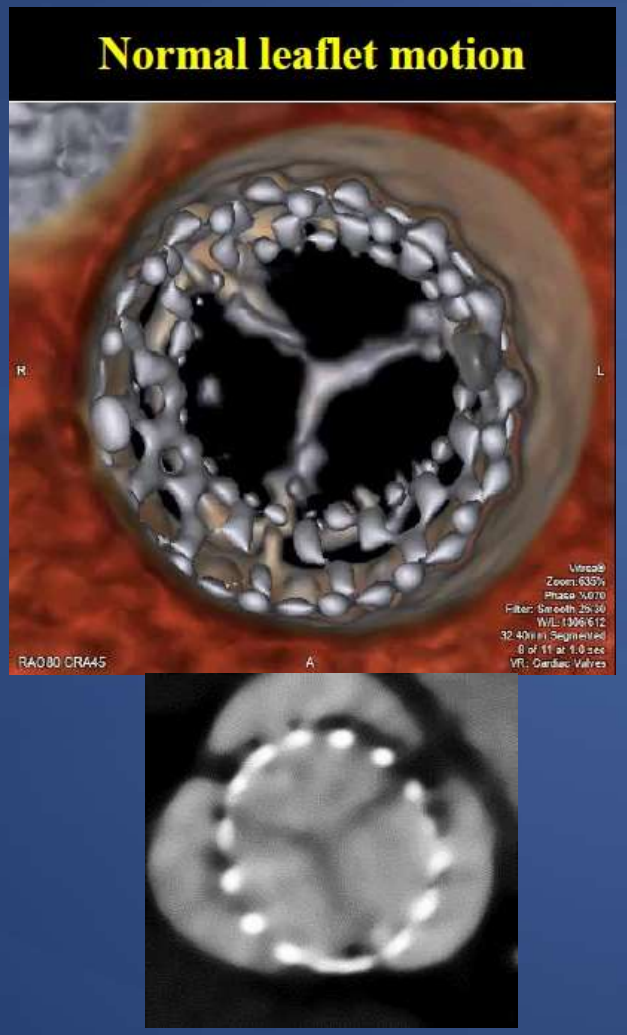
Abnormal Leaflet Findings in Bioprostheses

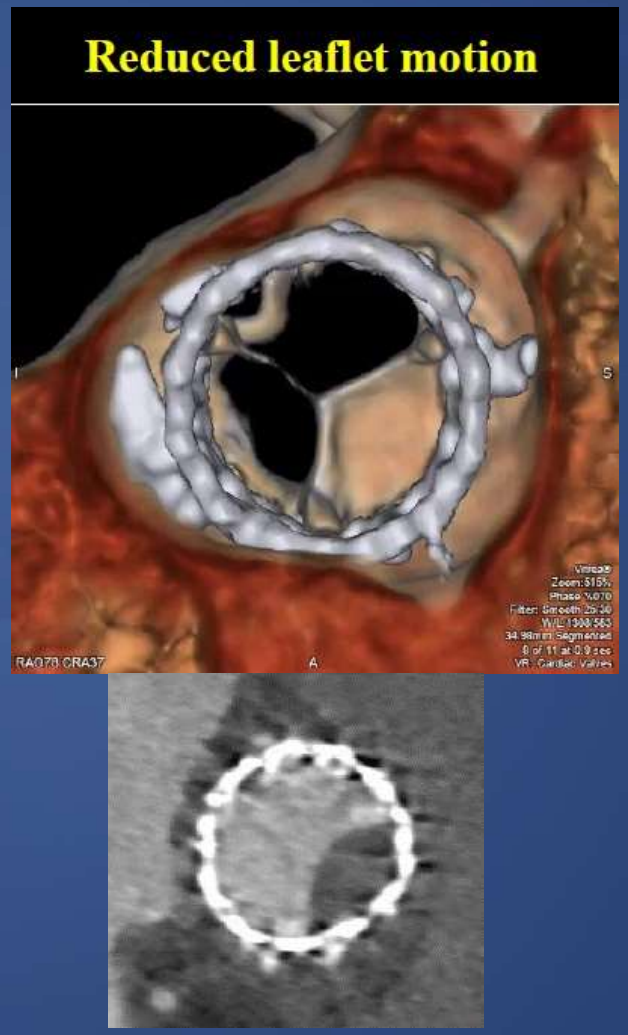
Authors	Diagnostic Method	Procedure	Finding	Patients, n	Finding, n (%)	Comment
Makkar et al[1]	MDCT	TAVR	Reduced leaflet motion	55	22 (40)	Surveillance
	MDCT	SAVR	Reduced leaflet motion	132	17 (13)	For cause
De Marchena et al[4]	Autopsy/surgery	TAVR	Valve thrombosis	4	4 (100)	For cause
Leetmaa et al[7]	MDCT	TAVR	Valve thrombosis	140	5 (4)	Surveillance
Brown et al[11]	Surgery	SAVR	Valve thrombosis	4568	8 (0.2)	For cause
Egbe et al[8]	Surgery	SAVR	Valve thrombosis		46	For cause
Del Trigo et al[16]	TTE	TAVR	Valve hemodynamic deterioration	1521	68 (4.5)	Surveillance
Jander et al[18]	TTE	SAVR	Valve hemodynamic deterioration	1751	17 (1)	Surveillance
Vemulapalli et al[19]	TTE	TAVR	Valve hemodynamic deterioration	10099	212 (2.1)	Surveillance, 30 d
	TTE	TAVR	Valve hemodynamic deterioration	3175	79 (2.5)	Surveillance, 1 y
Latib et al[15]	TTE	TAVR	Valve thrombosis	4266	26 (0.61)	Surveillance, mean 181 d
Pache et al[27]	MDCT	TAVR	HALT	156	16 (10.3)	Surveillance
Hansson et al[28]	MDCT	TAVR	HALT	405	28 (7)	Surveillance

David R. Holmes and Michael J. Mack. Circulation 2017.

Reduced leaflet motion

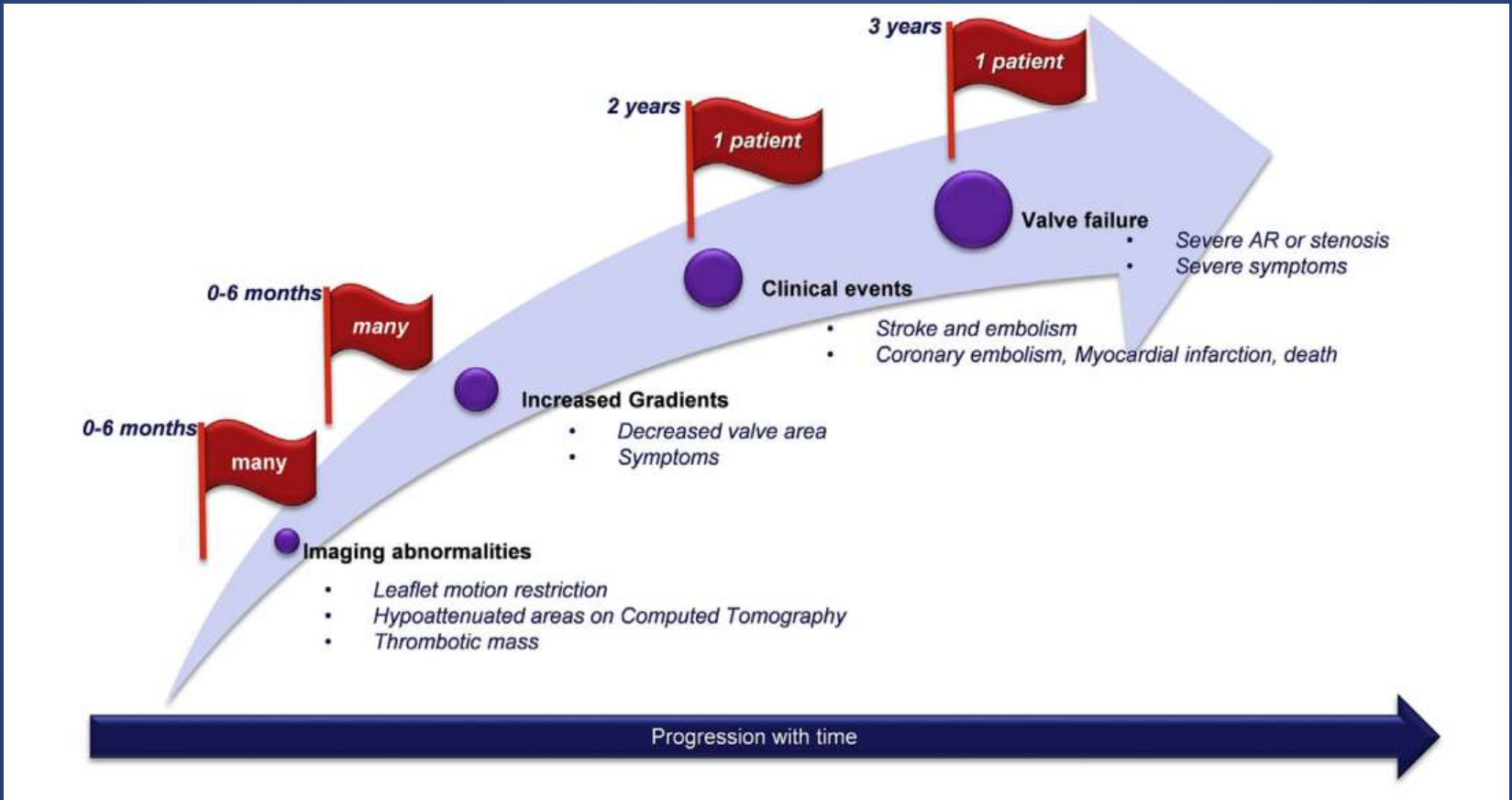
At least 50% restriction of leaflet motion of at least 50%





Chakravarty T, et al. Lancet. 2017 Mar 19. [Epub ahead of print]

Hypothetical Natural History of Transcatheter Valve Thrombosis



Marco Spaziano and Philippe Genereux et al. JACC 2014

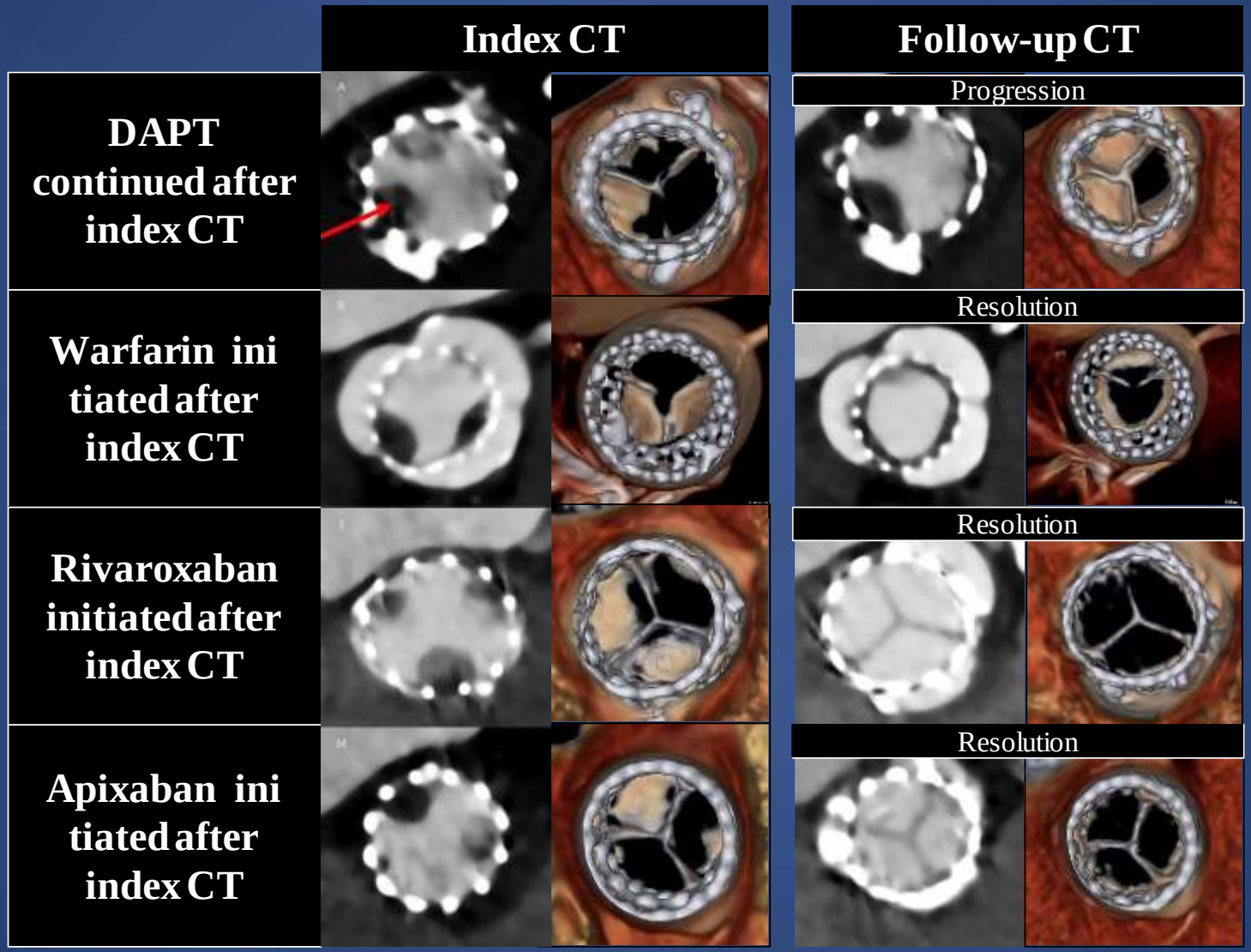
Predictors of Clinical Transcatheter Valve Thrombosis

TABLE 3 Predictors of Clinical Transcatheter Valve Thrombosis

	Odds Ratio (95% CI)	p Value
Male	0.7 (0.2–2.1)	0.53
Age >80 yrs	0.8 (0.3–2.2)	0.65
Systemic hypertension	1.1 (0.3–4.5)	0.85
Atrial fibrillation	1.8 (0.4–7.1)	0.43
Type 2 diabetes mellitus	0.2 (0.1–1.1)	0.06
Obesity (BMI >30 kg/m^2)	4.6 (1.6–13.1)	0.005
Presence of coronary artery disease	0.8 (0.3–2.3)	0.68
Antiplatelet therapy alone	79.1 (3.1–1,994.5)	0.008
Use of balloon-expandable valve	8.0 (2.1–29.7)	0.002
Valve-in-valve procedure	17.1 (3.4–84.9)	0.001
Pre-dilatation	0.9 (0.3–2.8)	0.81
Post-dilatation	1.2 (0.3–4.7)	0.76

Marco Spaziano and Philippe Genereux et al. JACC 2014

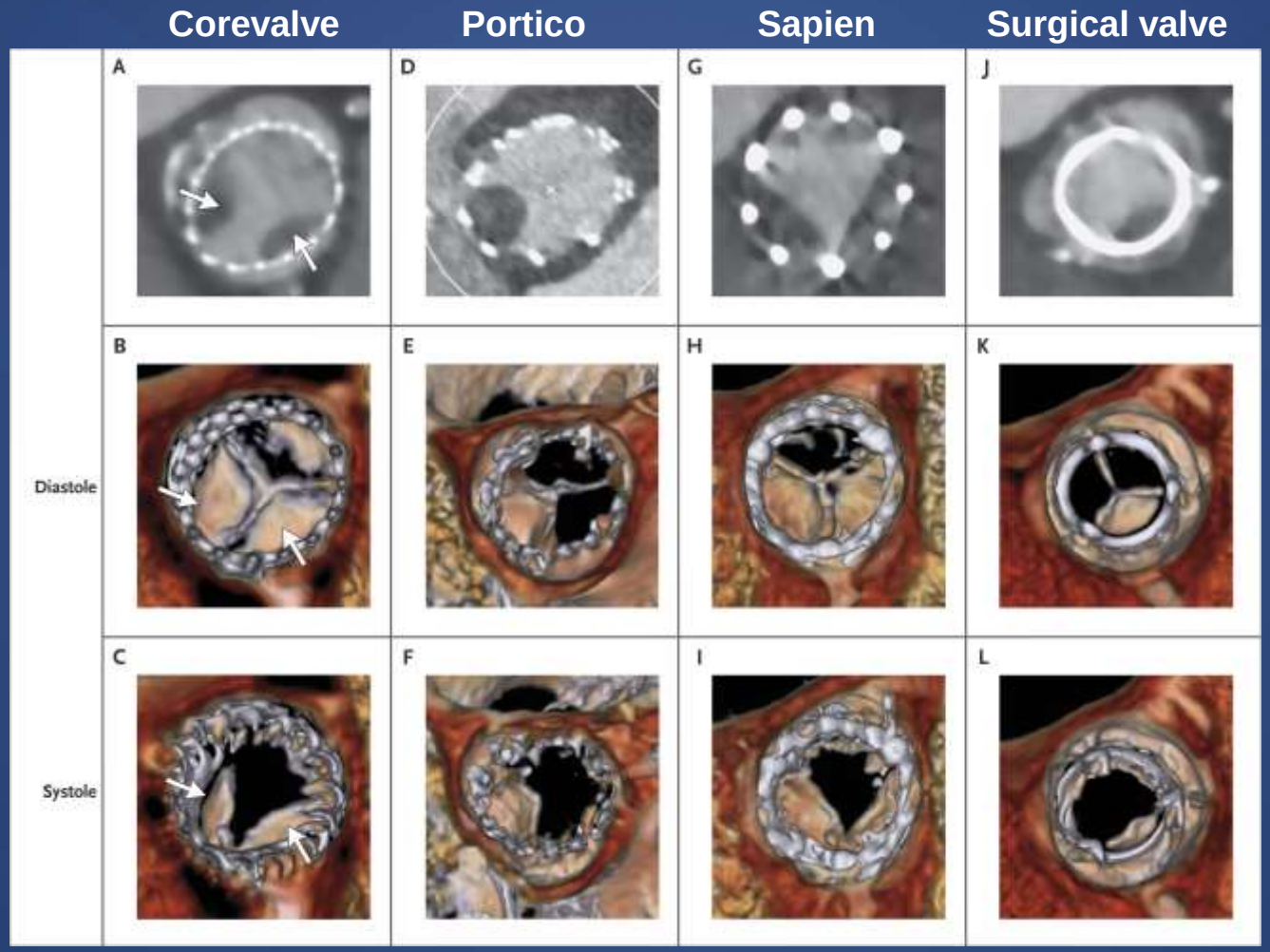
Anticoagulation vs. DAPT



Chakravarty T, et al. Lancet 2017.

Possible Subclinical Leaflet Thrombosis in Bioprosthetic Aortic Valves

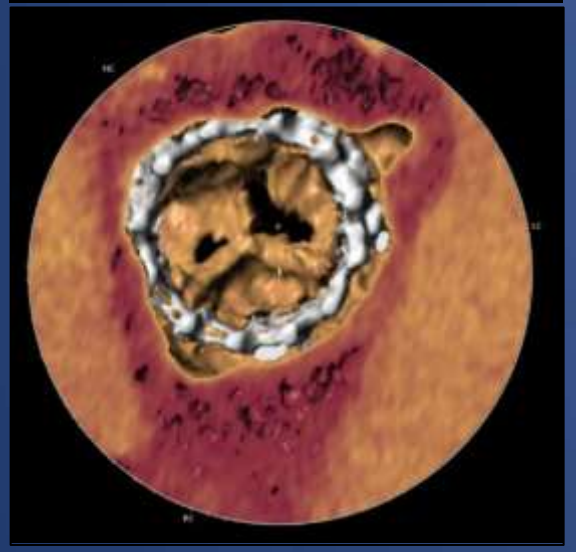
Evidence of Reduced Leaflet Motion in Multiple Prosthesis Types



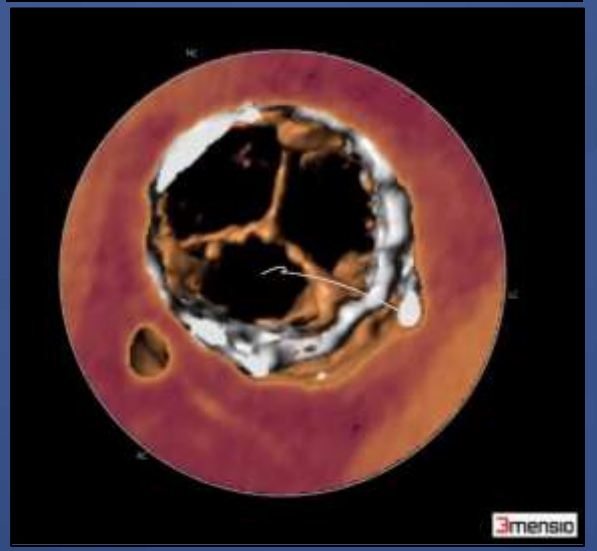
Makkar RR et al. N Engl J Med 2015;373:2015-2024

Recurrence of Reduced Leaflet Motion Following Discontinuation of anticoagulation

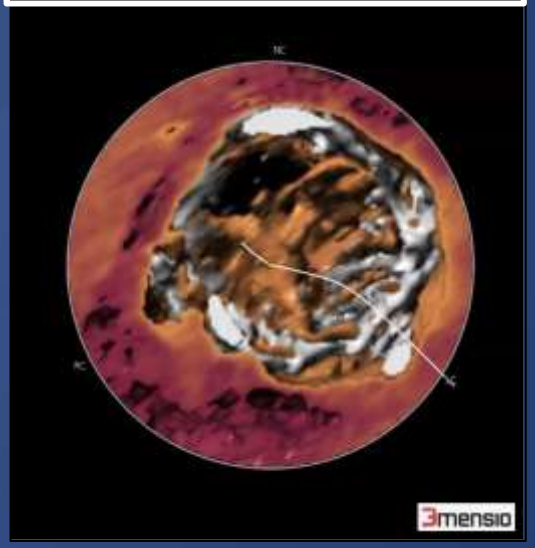
Baseline
Reduced leaflet motion



s/p Xarelto 10mg
Normal leaflet motion



Six months following discontinuation of x arelto
Reduced leaflet motion



Chakravarty T, et al. Lancet 2017.

Subclinical leaflet thrombosis in surgical and transcatheter bioprosthetic aortic valves: an observational study

Study Design

657 patients underwent CTs in the RESOLVE registry Cedars-Sinai Medical Center, Los Angeles

274 patients underwent CTs in the SAVORY registry Rigshospitalet, Copenhagen

931 patients undergoing CTs

890 patients with interpretable CTs were included in the analysis
RESOLVE registry: 626 patients
SAVORY registry: 264 patients
Median time from AVR to CT 83 days (IQR 32-281 days)

752 transcatheter valves
Median time from TAVR to CT
58 days (IQR 32–236 days)

138 surgical valves
Median time from SAVR to CT
162 days (IQR 79–417 days)

Time from TAVR to CT vs. SAVR to CT: p<0.0001

Chakravarty T, et al. Lancet. 2017 Mar 19. [Epub ahead of print]

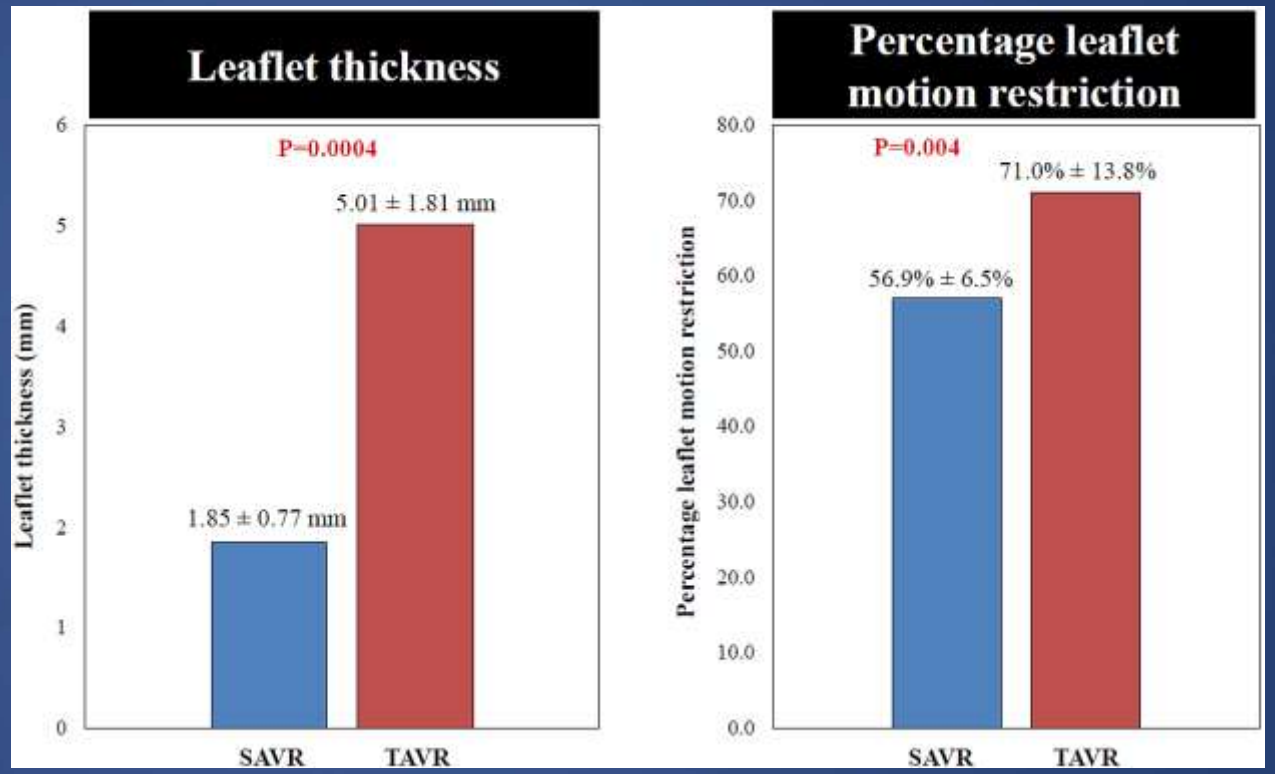
Prevalence of reduced leaflet motion

Transcatheter vs. surgical bioprosthetic aortic valves: p=0.001

Reduced leaflet motion 106 (11.9%) patients

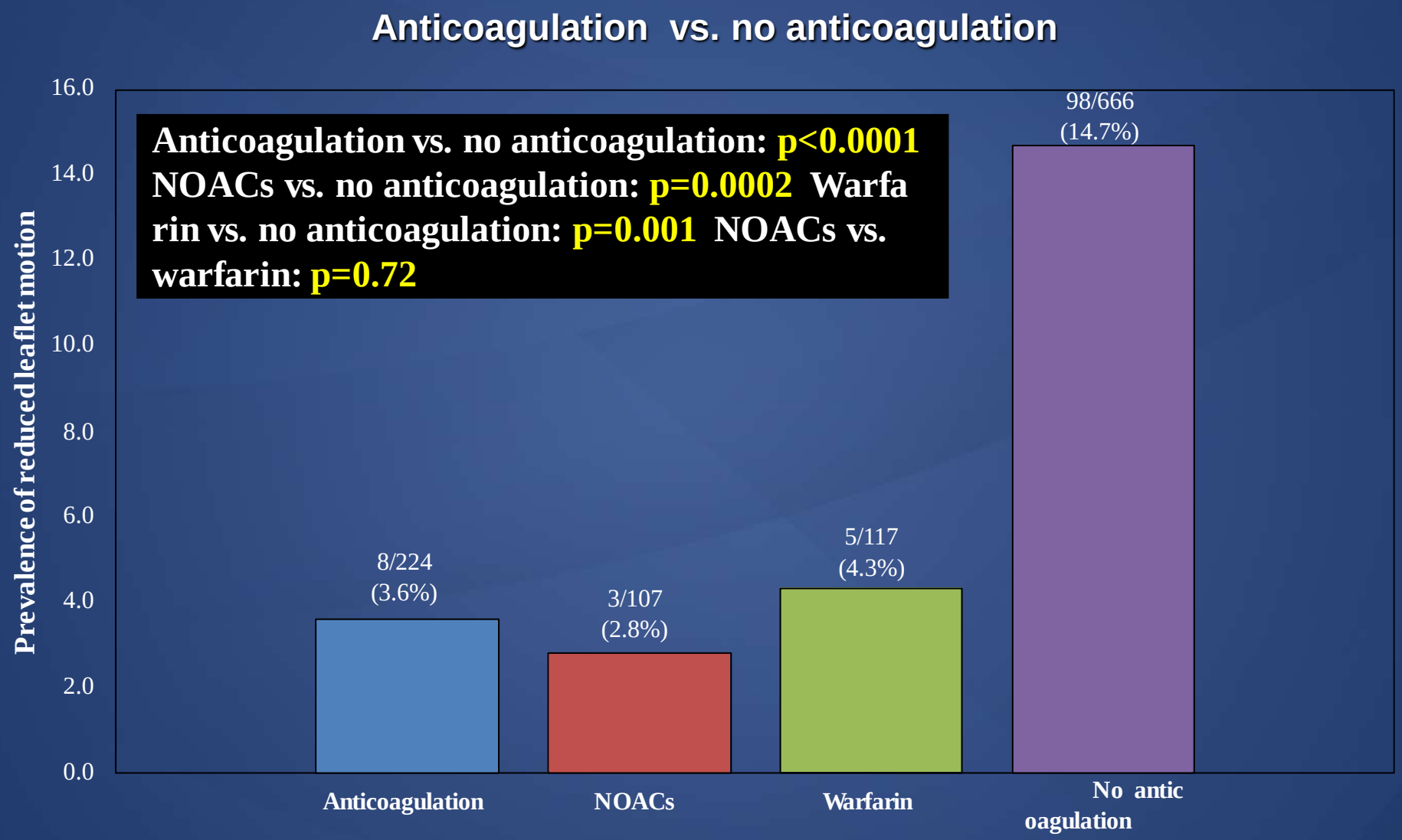
Transcatheter valves
13.4% (101 out of 752)

Surgical valves
3.6% (5 out of 138)



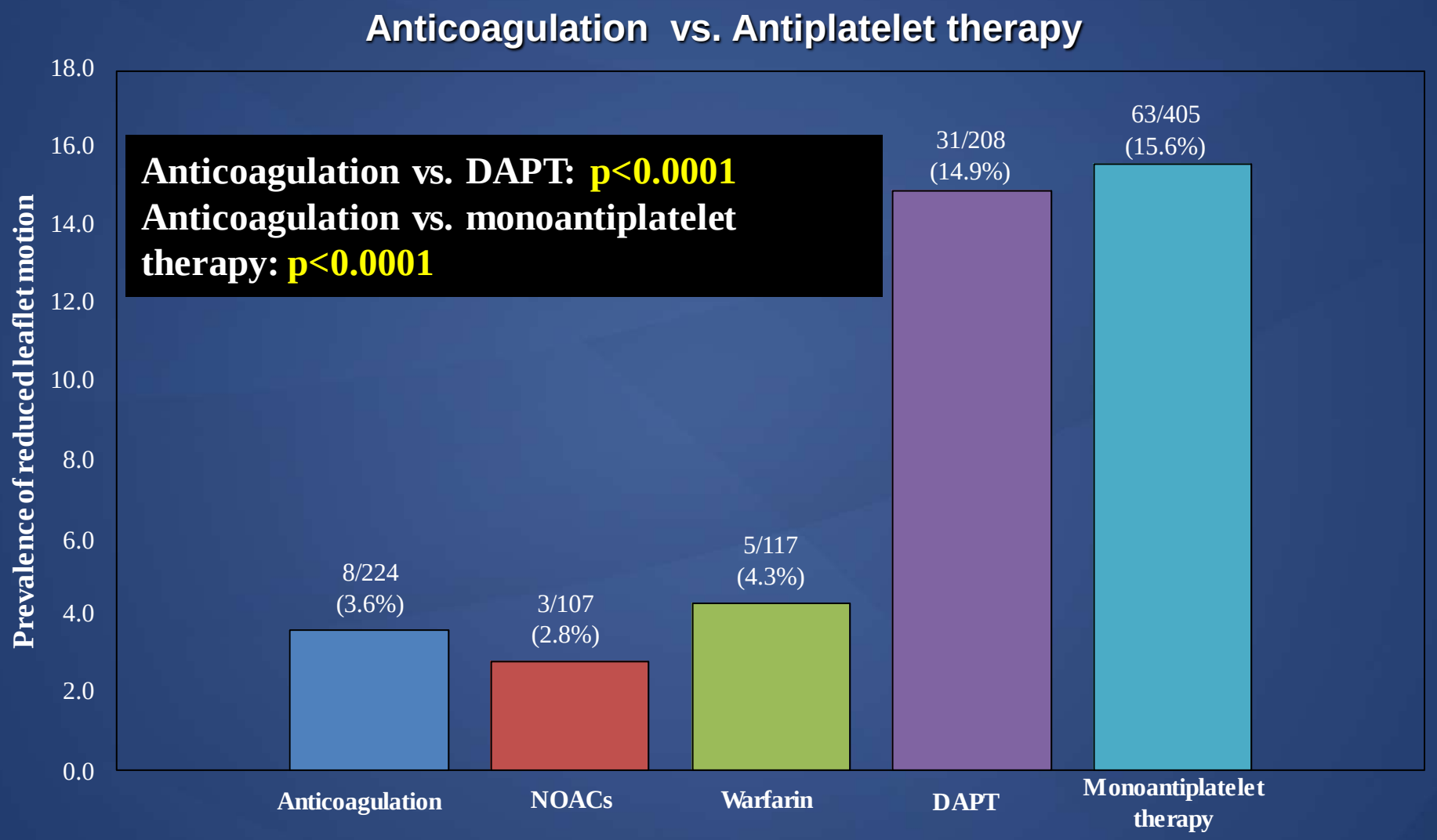
Chakravarty T, et al. Lancet. 2017 Mar 19. [Epub ahead of print]

Anticoagulation and Reduced Leaflet Motion



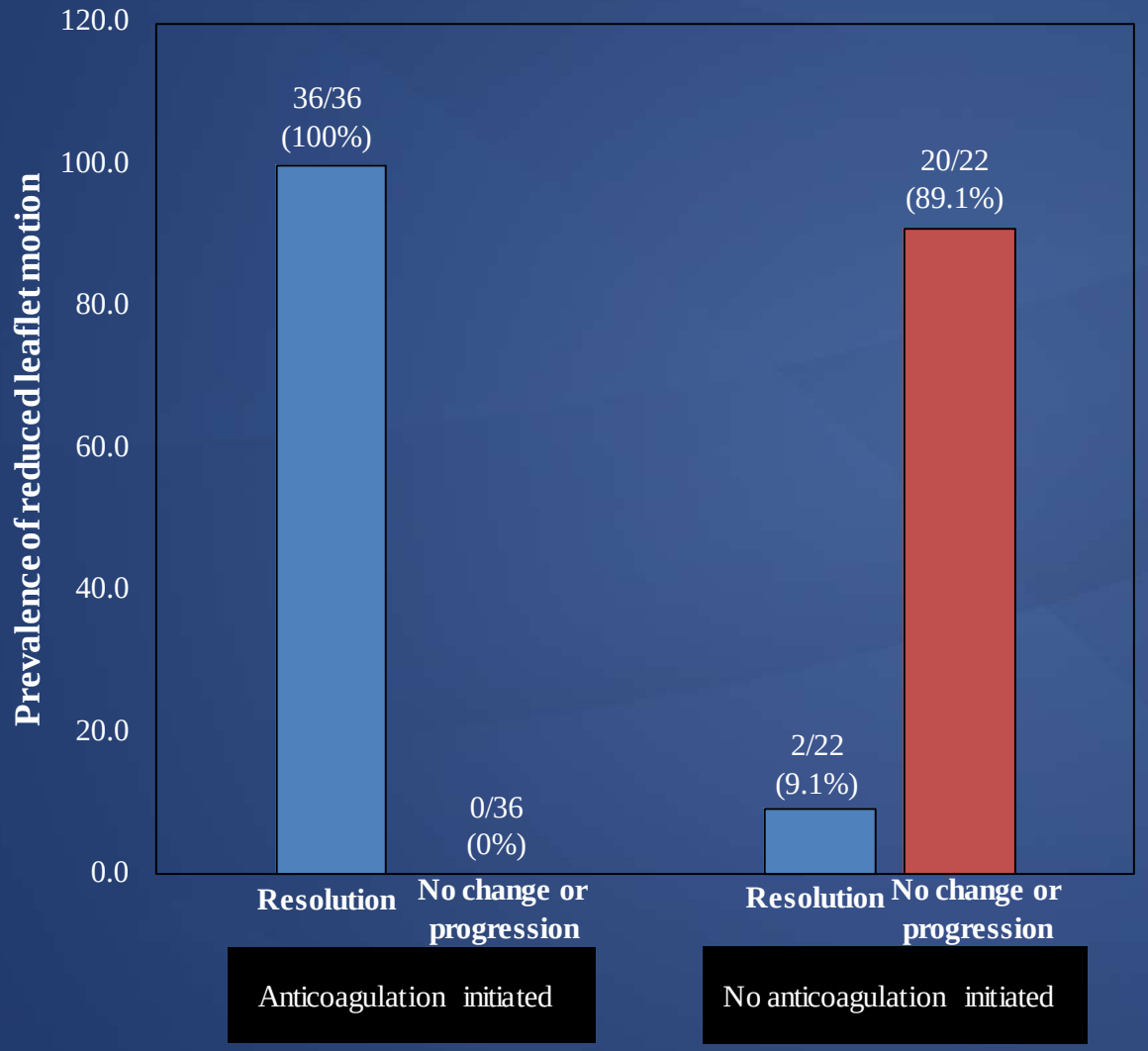
Chakravarty T, et al. Lancet 2017.

Anticoagulation and Reduced Leaflet Motion



Chakravarty T, et al. Lancet 2017.

Impact of Initiation of Anticoagulation on Reduced Leaflet Motion

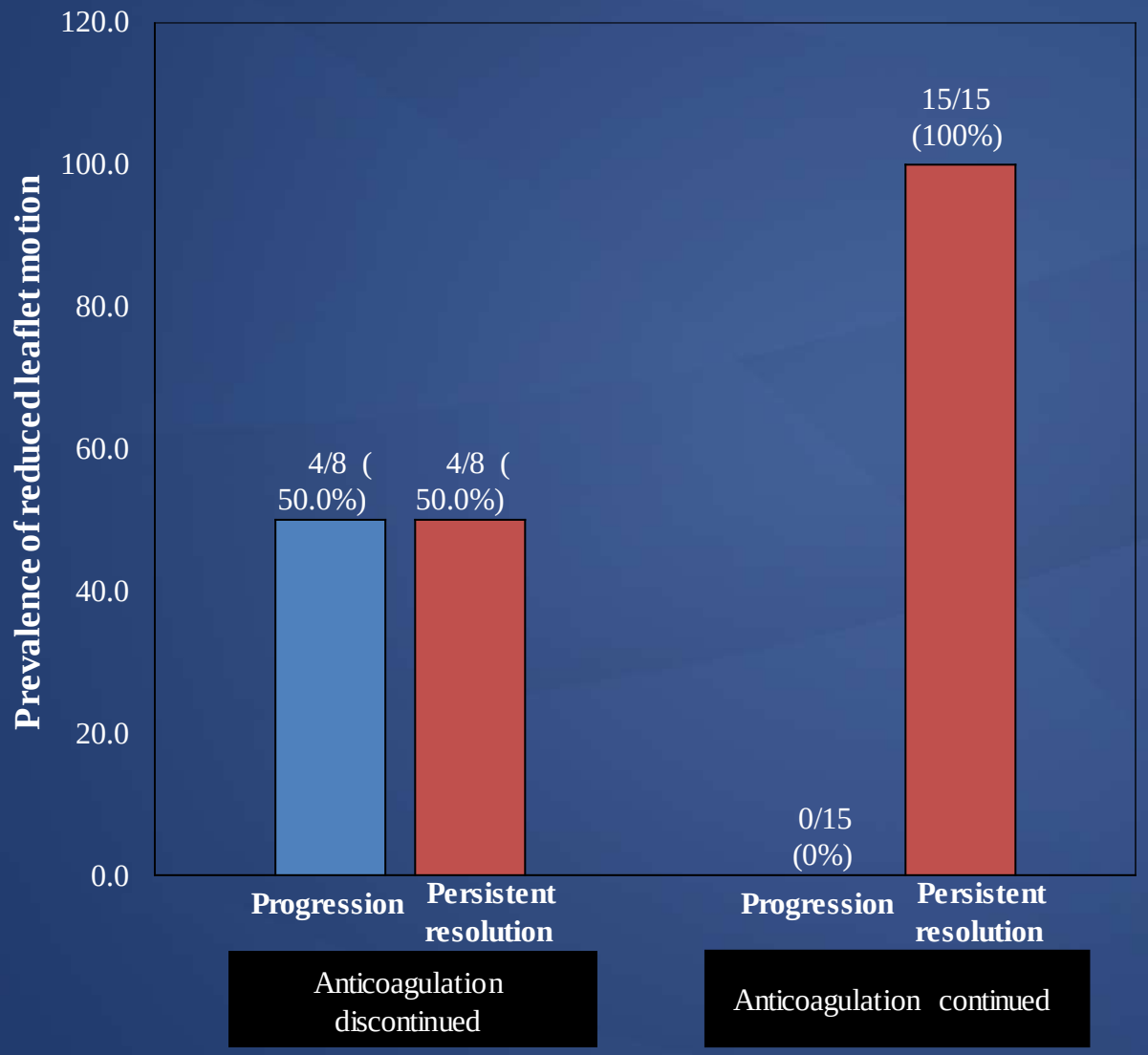


- **Resolution in 36 out of 36 patients** treated with anti coagulation (NO ACs, n=12; warf arin, n=24)
- **Persistence/progres sion in 20 out of 22 patients** not treated with anticoagulati on

P<0.0001

Chakravarty T, et al. Lancet 2017.

Impact of Discontinuation of Anticoagulation Following Resolution of Reduced Leaflet Motion

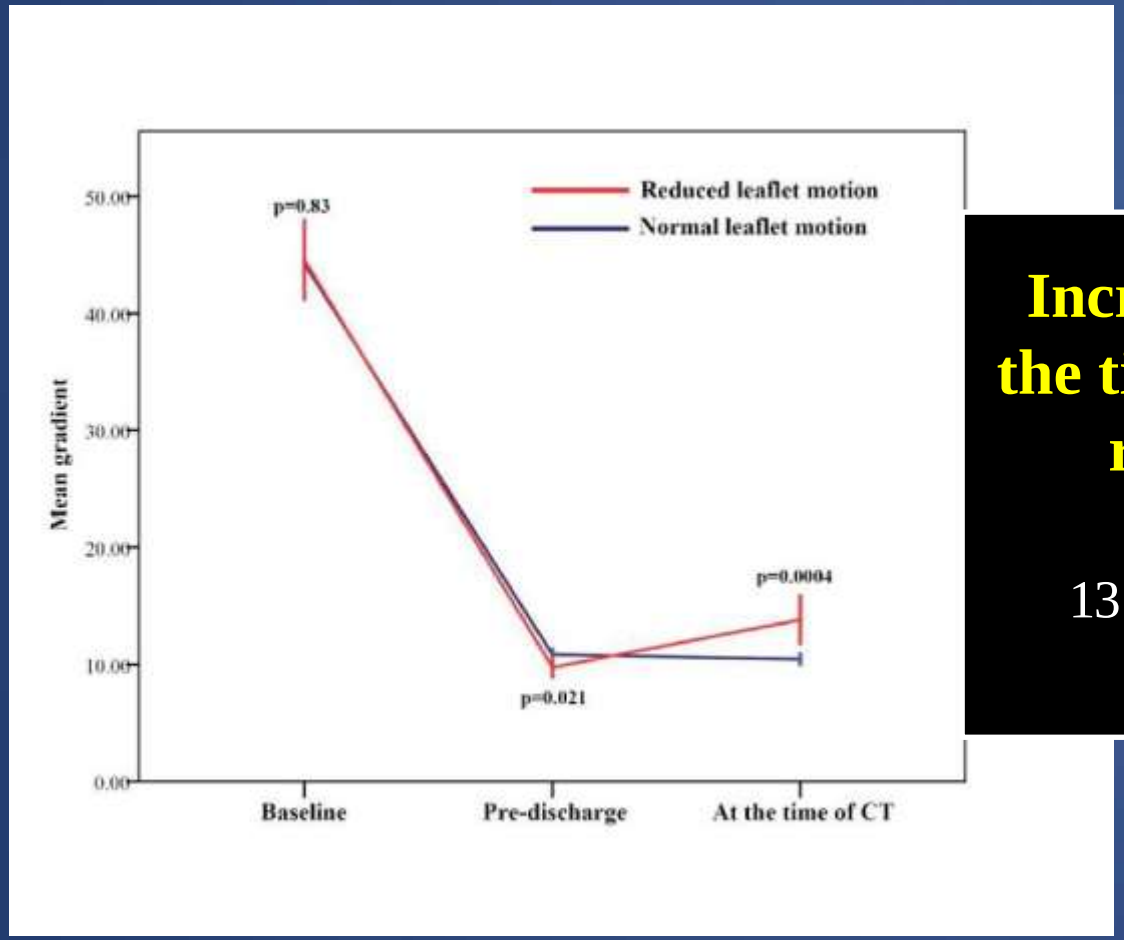


- Reduced leaflet motion **recurred in 4 out of 8 patients** in whom anticoagulation was discontinued
- Reduced leaflet motion **did not recur in the 15 patients** who were continued on anticoagulation

P=0.008

Chakravarty T, et al. Lancet 2017.

Impact of Reduced Leaflet Motion on Valve Hemodynamics

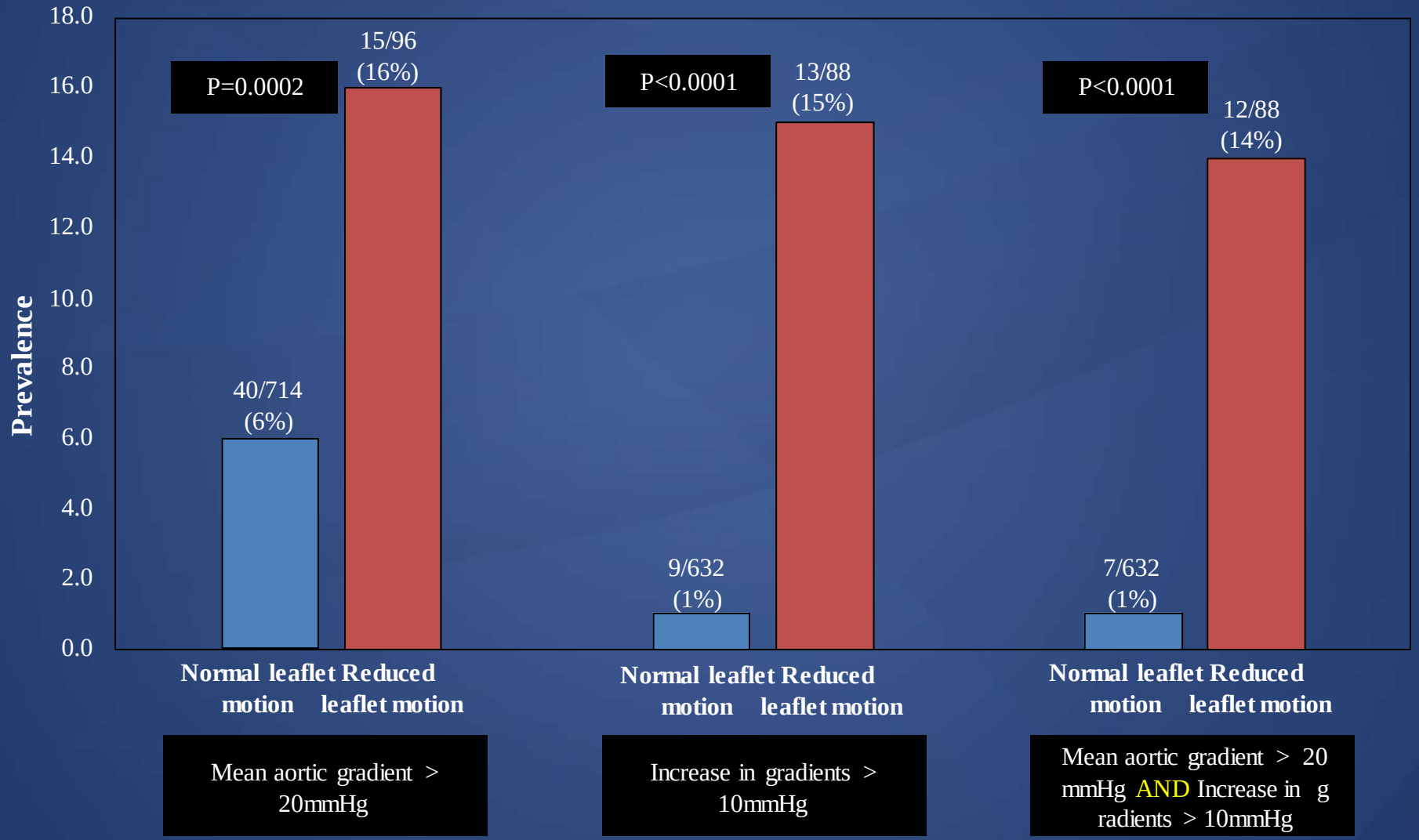


Increased mean gradients at the time of CT in patients with reduced leaflet motion

13·8±10·0 mmHg vs. 10·4±6·3 mmHg, p=0.0004

Chakravarty T, et al. Lancet 2017.

Increased Gradients in patients with Reduced Leaflet Motion



Chakravarty T, et al. Lancet 2017.

Impact of Reduced Leaflet Motion on Clinical Outcomes

Only Non-Procedural Events (>72 Hours Post-TAVR/SAVR) included

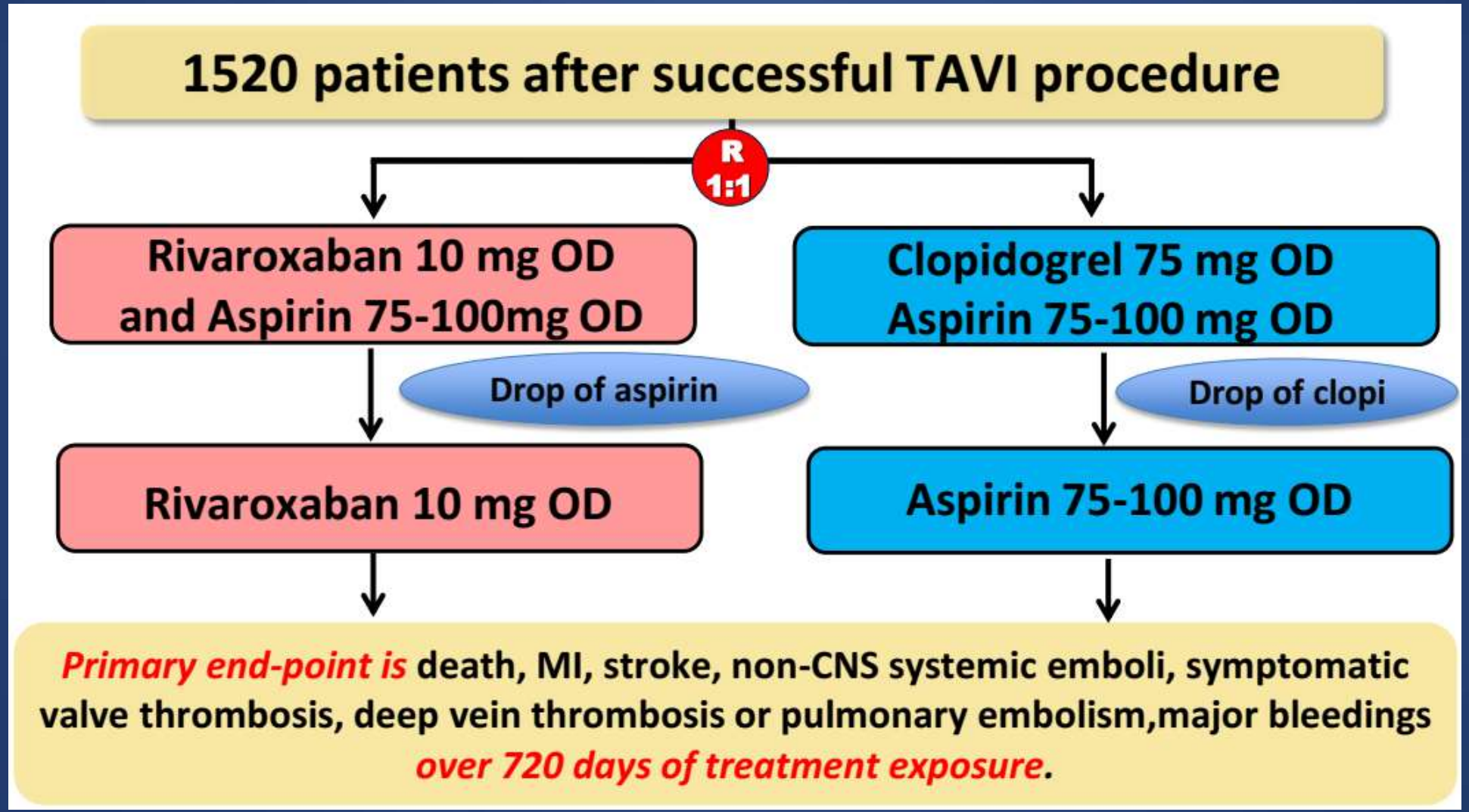
	Normal leaflet motion (N=784)		Reduced leaflet motion (N=106)			
Non-procedural events	n/N (%)	Rate per 100 person-years	n/N (%)	Rate per 100 person-years	Hazard ratio (95% CI)	p-value
Death	34/784 (4·3%)	2·91	4/106 (3·8%)	2·66	0·96 (0·34-2·72)	0·94
Myocardial infarction	4/784 (0·5%)	0·34	1/106 (0·9%)	0·67	1·91 (0·21-17·08)	0·56
Strokes/TIAs	20/784 (2·6%)	1·75	8/106 (7·6%)	5·71	3·30 (1·45-7·50)	0·004
All strokes*	15/784 (1·9%)	1·31	4/106 (3·8%)	2·75	2·14 (0·71-6·44)	0·18
Ischemic strokes	14/784 (1·8%)	1·22	4/106 (3·8%)	2·75	2·29 (0·75-6·97)	0·14
TIAs	7/784 (0·9%)	0·60	5/106 (4·7%)	3·48	5·89 (1·87-18·60)	0·002

- No significant difference in strokes; but increased risk of TIAs and strokes/TIAs
- TIA=Transient ischemic attack/ * All strokes include hemorrhagic and ischemic strokes

Chakravarty T, et al. Lancet 2017.

Rivaroxaban vs. DAPT after TAVR

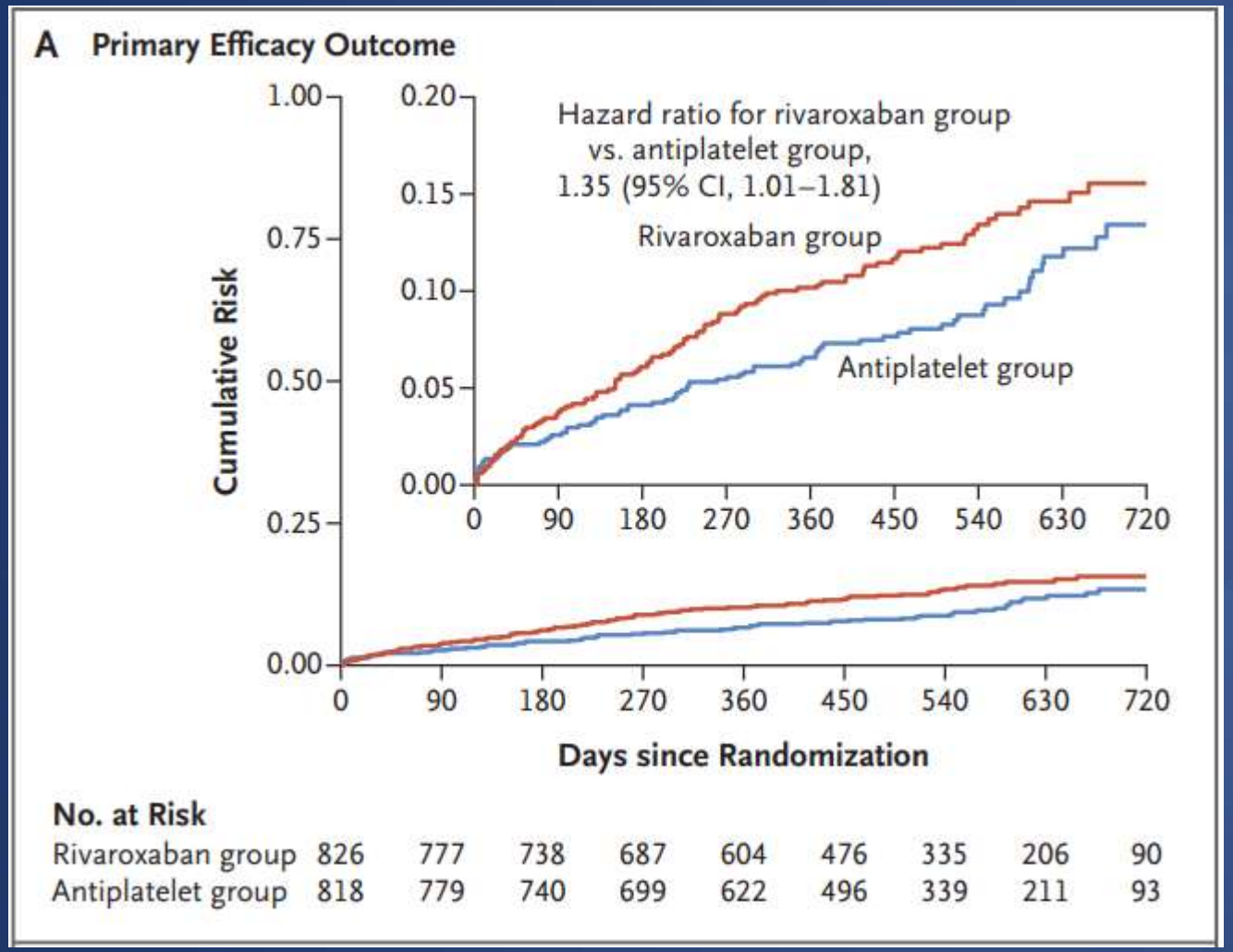
GALILEO Study



Stephan Windecker et al. Am Heart J 2017.

Rivaroxaban vs. DAPT after TAVR

GALILEO Study



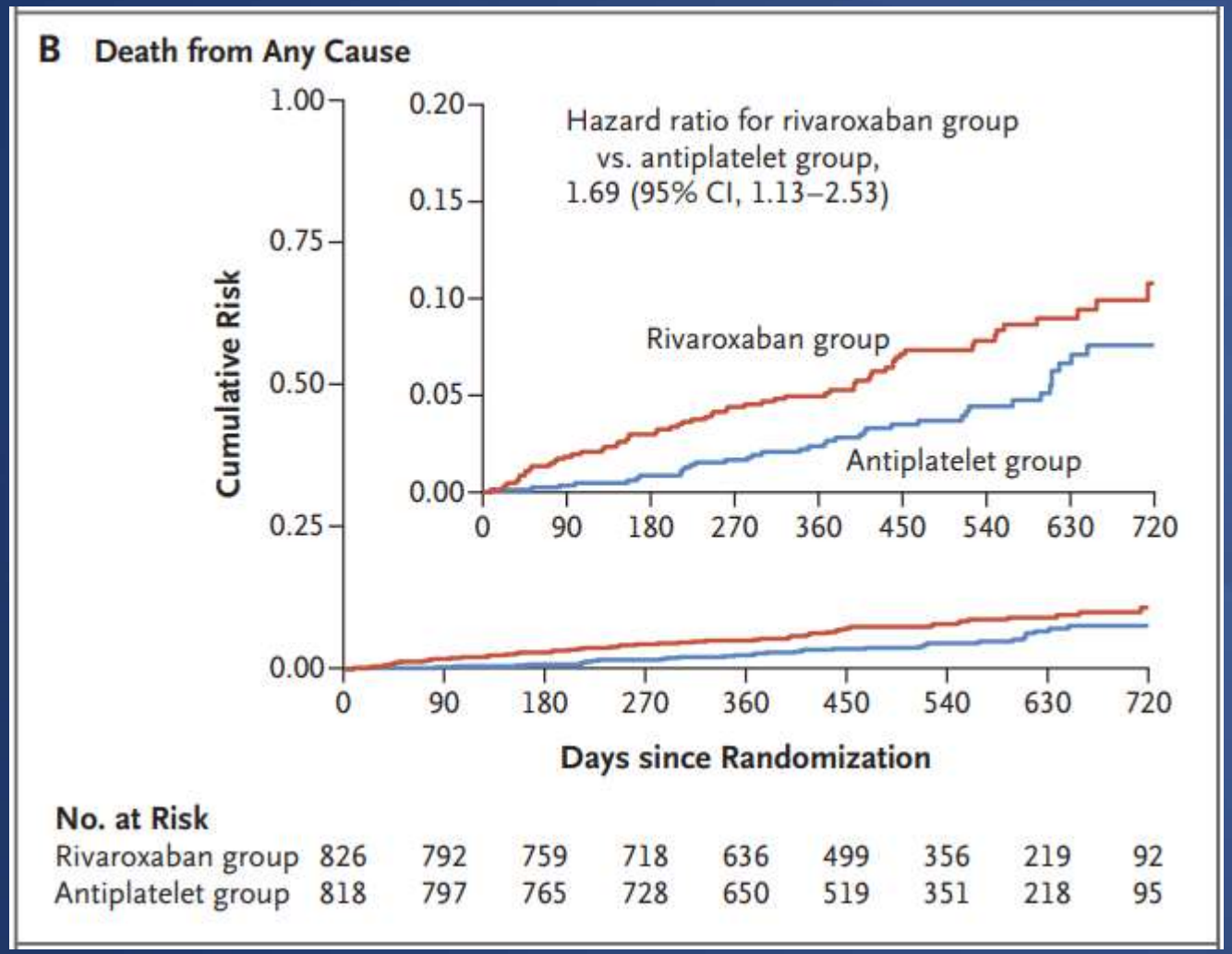
Primary Efficacy Outcomes

Death, stroke, MI, symptomatic valve thrombosis, PTE, DVT, systemic embolism

G.D. Dangas et al. N Engl J Med 2020;382:120-9

Rivaroxaban vs. DAPT after TAVR

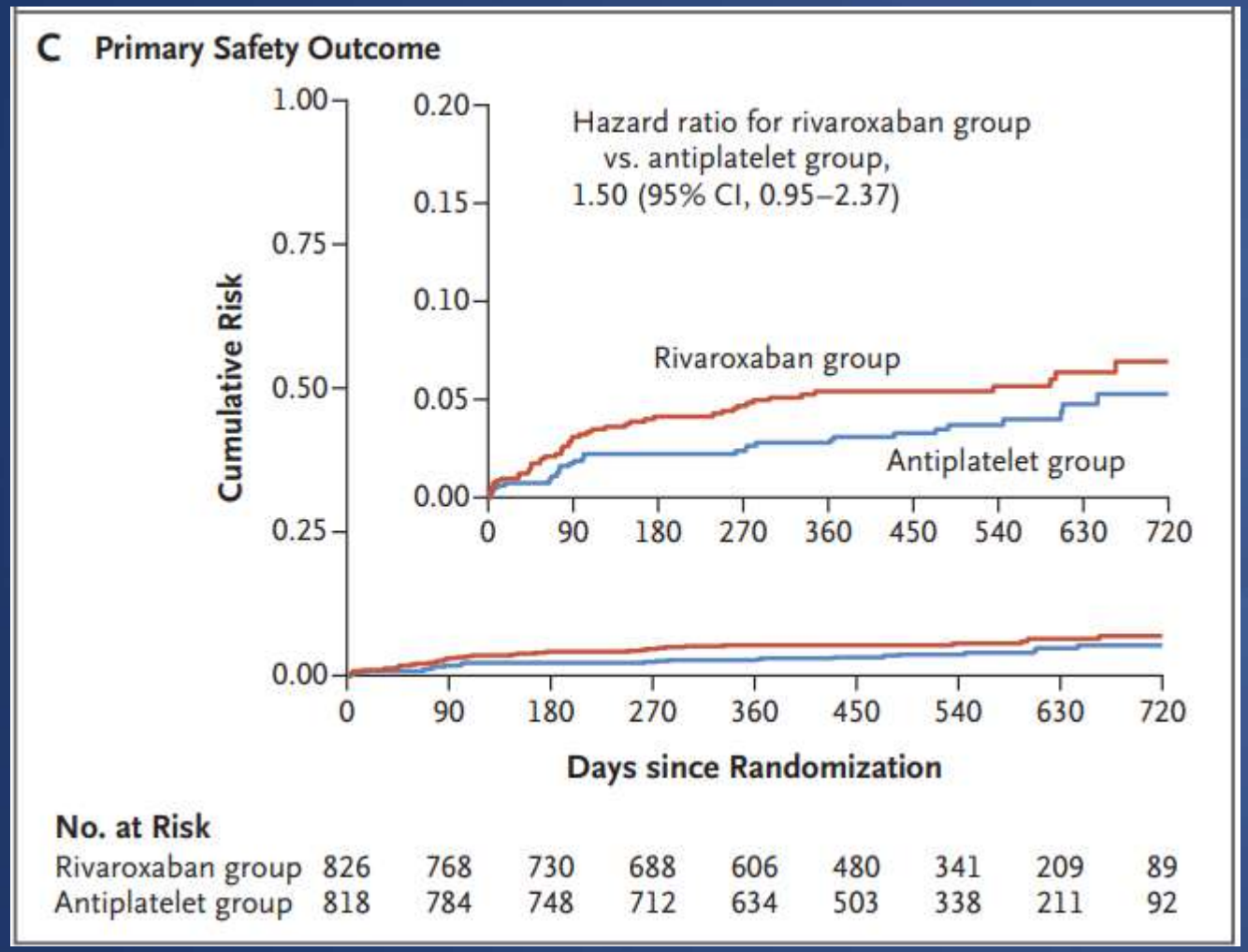
GALILEO Study



G.D. Dangas et al. N Engl J Med 2020;382:120-9

Rivaroxaban vs. DAPT after TAVR

GALILEO Study



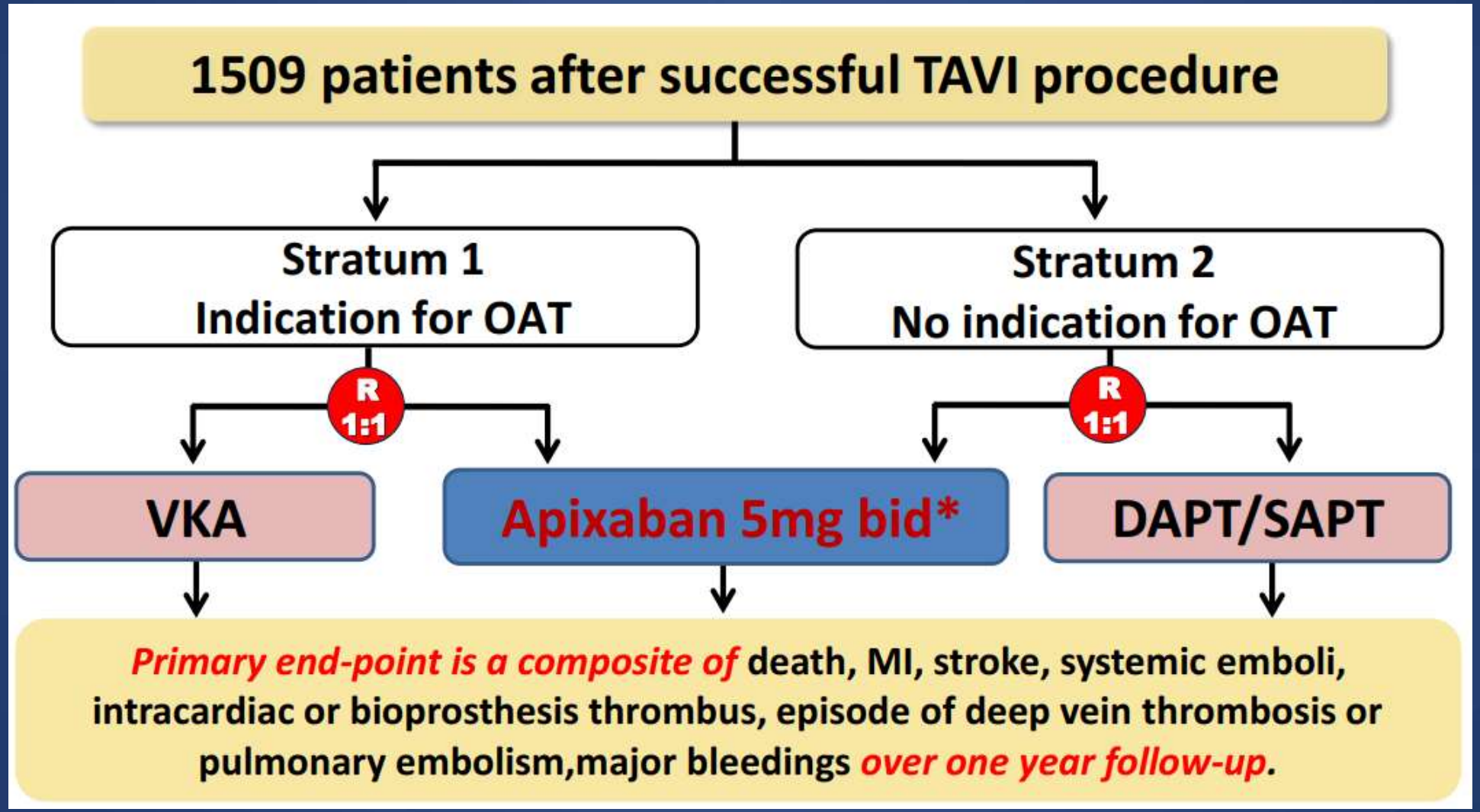
Primary Safety Outcomes

VARC life-threatening, disabling, or major bleeding

G.D. Dangas et al. N Engl J Med 2020;382:120-9

Apixaban vs. VKA vs. DAPT after TAVR

ATLANTIS Study



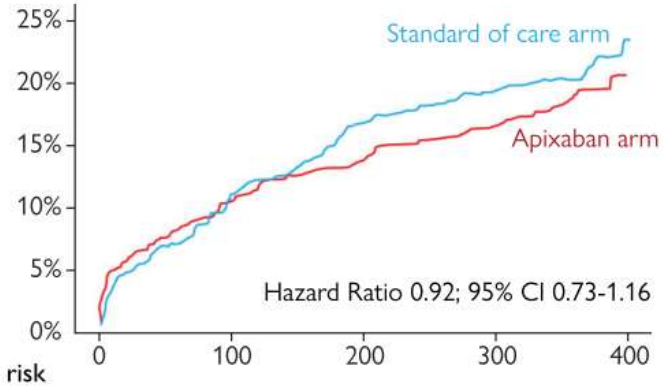
Jean-Philippe Collet et al. Am Heart J 2018.

Apixaban vs. VKA vs. DAPT after TAVR

The ATLANTIS trial

Primary endpoint (Intent-to-treat)

Time to death, stroke, MI, systemic embolim, intracardiac or valve thrombosis, VT/PE, major bleedings



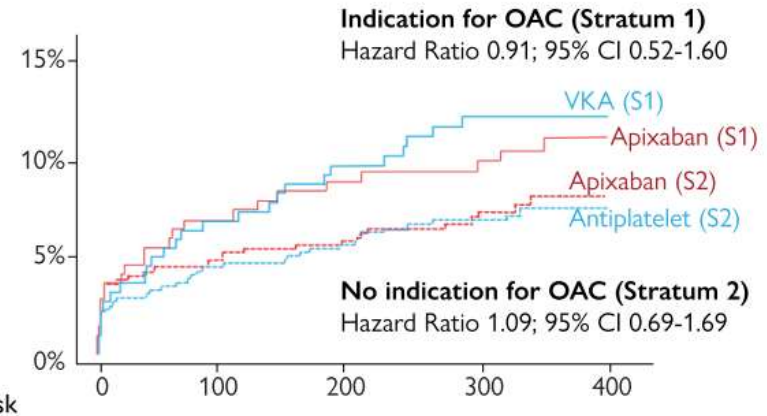
No at risk					
SOC	751	646	583	555	42
Apixaban	749	645	612	585	27

	Apixaban (n= 749)	Standard-of-care (n= 751)	P_{int}	Hazard ratio (95% CI)
Primary outcome	138 (18.4%)	151 (20.1%)		0.92 (0.73-1.16)
No indication for OAC (n=1049)	89 (16.9%)	101 (19.3%)	0.57	0.88 (0.66-1.17)
Indication for OAC (n=451)	49 (21.9%)	50 (21.9%)		1.02 (0.68-1.51)

- Per-protocol analysis (n=1299) were consistent with ITT analyses for the primary endpoint (HR 0.98; 95% CI 0.71-1.13)
- Non-inferiority of apaxiban versus the atandard of care was demonstrated for the primary endpoint using a prespecified non-inferiority margin for the upper boundary of the hazard ratio of 1,2

Safety analysis

(Primary safety : BARC 4, 3a, 3b and 3c)

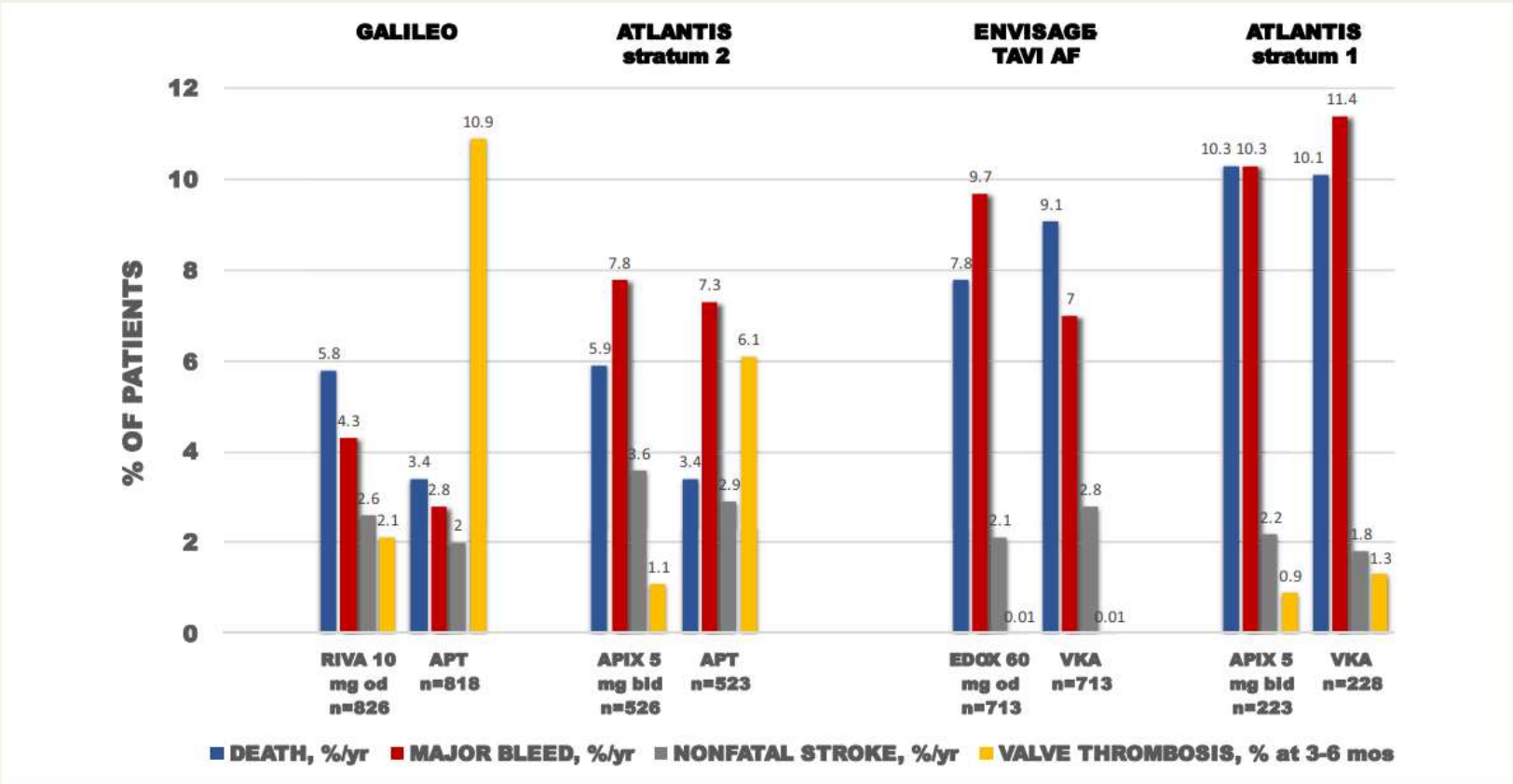


No at risk					
VKA (S1)	228	196	180	170	14
Apixaban (S1)	223	188	177	167	10
Antiplat(S2)	526	479	459	441	18
Apixaban (S2)	523	480	457	441	31

	Apixaban (n= 749)	Standard-of-care (n= 751)	Hazard ratio (95% CI)
Primary safety endpoint†	64 (8.5%)	64 (8.5%)	1.02 (0.72-1.44)
Life-threatening bleeding	19 (2.5%)	18 (2.4%)	1.06 (0.55-2.02)
Major bleeding	50 (6.7%)	48 (8.4%)	1.07 (0.72-1.59)
Major bleeding (BARC 2 or 3a)	70 (9.3%)	78 (10.4%)	0.91 (0.66-1.26)
Any bleeding†	174 (23.2%)	170 (22.6%)	1.05 (0.85-1.30)

†Life-threatening (including fatal) or disabling or major bleeding (BARC 4, 3a, 3b and 3c), as defined by Valve Academic Research Consortium-2 (VARC-2).

Jean-Philippe Collet et al. Eur Heart J 2022;43:2783-2797



Graphical Abstract **Major outcomes of randomized controlled trials investigating direct oral anticoagulants in patients undergoing successful TAVI.** 'Non-fatal stroke' refers to ischaemic stroke in GALILEO[5] and ENVISAGE-TAVI AF,[6] and to any stroke/transient ischaemic attack/systemic embolism in ATLANTIS.[13] 'Valve thrombosis' refers to RLM of >50% of ≥1 leaflet(s) (i.e. grade 3–4) in GALILEO,[8] to transprosthetic mean gradient ≥20 or ≥10 mmHg above previous measurements or HALT/RLM grade 3–4 in ATLANTIS,[13] and to thrombosis of haemodynamic relevance, symptomatic or completely reversible by high-intensity anticoagulation or to HALT/RLM or transprosthetic mean gradient ≥20 or ≥10 mmHg above previous measurements in ENVISAGE-TAVI AF.[6] Apix = apixaban; APT = antiplatelet therapy alone; bid = twice daily; Edox = edoxaban; HALT = hypo-attenuated leaflet thickening; od = once daily; Riva = rivaroxaban; RLM = reduced leaflet motion; VKA = vitamin K antagonist.

Felicita Andreotti et al. Eur Heart J 2022;43:2798-2800

ADAPT-TAVR Trial

Anticoagulant versus Dual Antiplatelet Therapy for Preventing Leaflet Thrombosis and Cerebral Embolization After Transcatheter Aortic Valve Replacement

Treatment Group

- **Edoxaban group**

  : Take 60 mg of edoxaban (Lixiana, Daiichi Sankyo, Korea) once daily for at least 6 months

  : 30mg once a day if Wt ≦ 60kg, renal insufficiency (15 ≤ CrCL ≤ 50 mL / min)

- **DAPT group**

  : Take aspirin (75-100 mg) and clopidogrel (75 mg) once daily for at least 6 months

Cardiac CT imaging

- For all patients enrolled in this trial, CT (four-dimensional, volume-rendered) will be performed at 6 months (± 1 month) after the index TAVR procedure to confirm the
- presence of the leaflet thrombosis of THV
- quantitative assessment of leaflet motion

- Leaflet motion; defined as normal, mildly reduced (<50% reduction), moderately reduced (50 to 70% reduction), severely reduced (>70% reduction), or immobile (lack of motion in at least one valve leaflet) in at least one valve leaflet

Brain MRI imaging

- For all patients enrolled in this trial, diffusion weighted (DW) brain MRI imaging using a 3-T scanner will be performed at 1-7 days and 6 months post-TAVR procedure

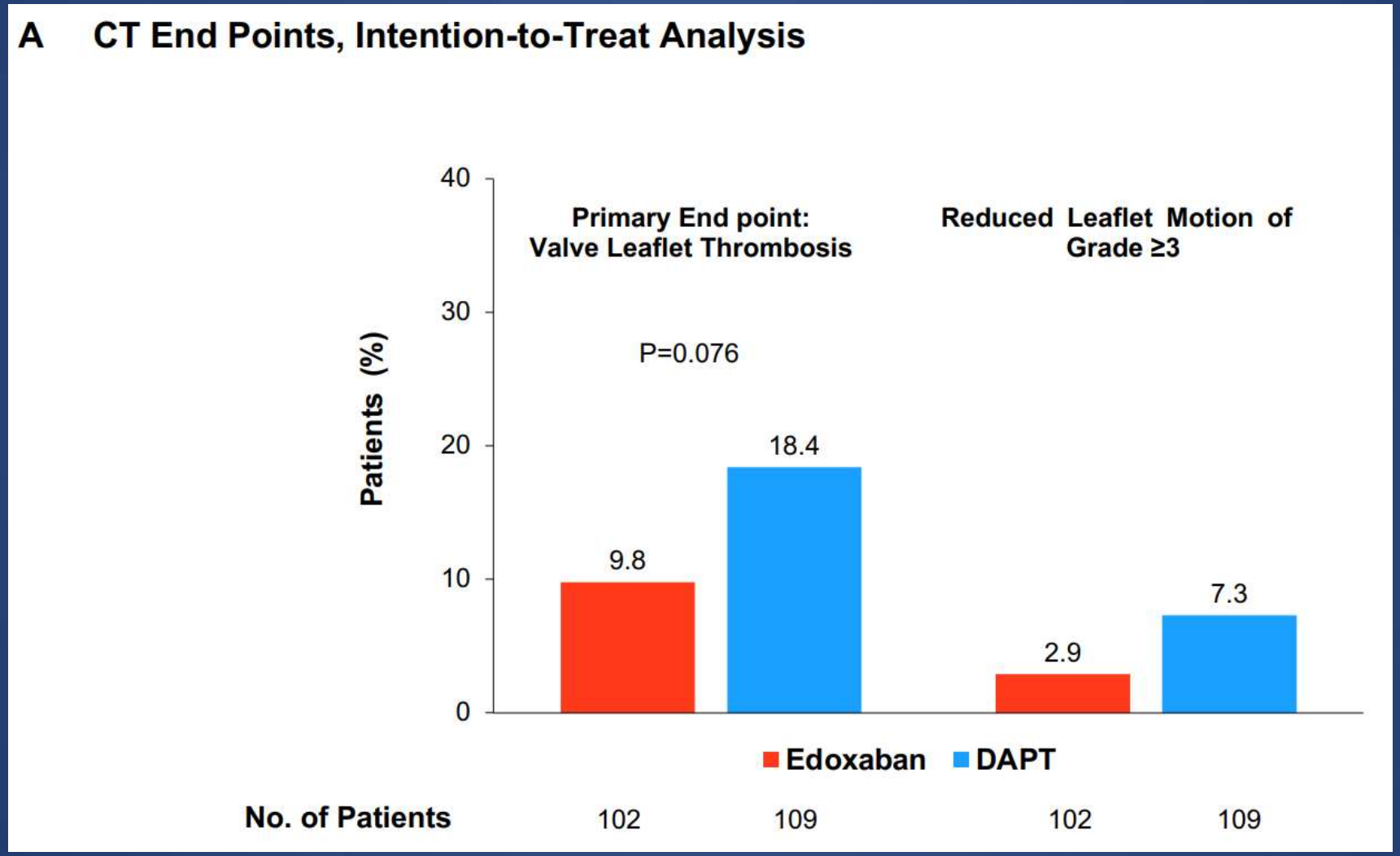
- Follow-up MRI imaging will be matched with immediate post-TAVR scans, and subtraction analyses are performed to identify new lesions in the entire brain. MRI outcomes included calculation of number and volume of new DWIs (postprocedure – 6 months) by subtraction of the existing baseline lesions in the whole brain.

Neurological and neurocognitive function assessment

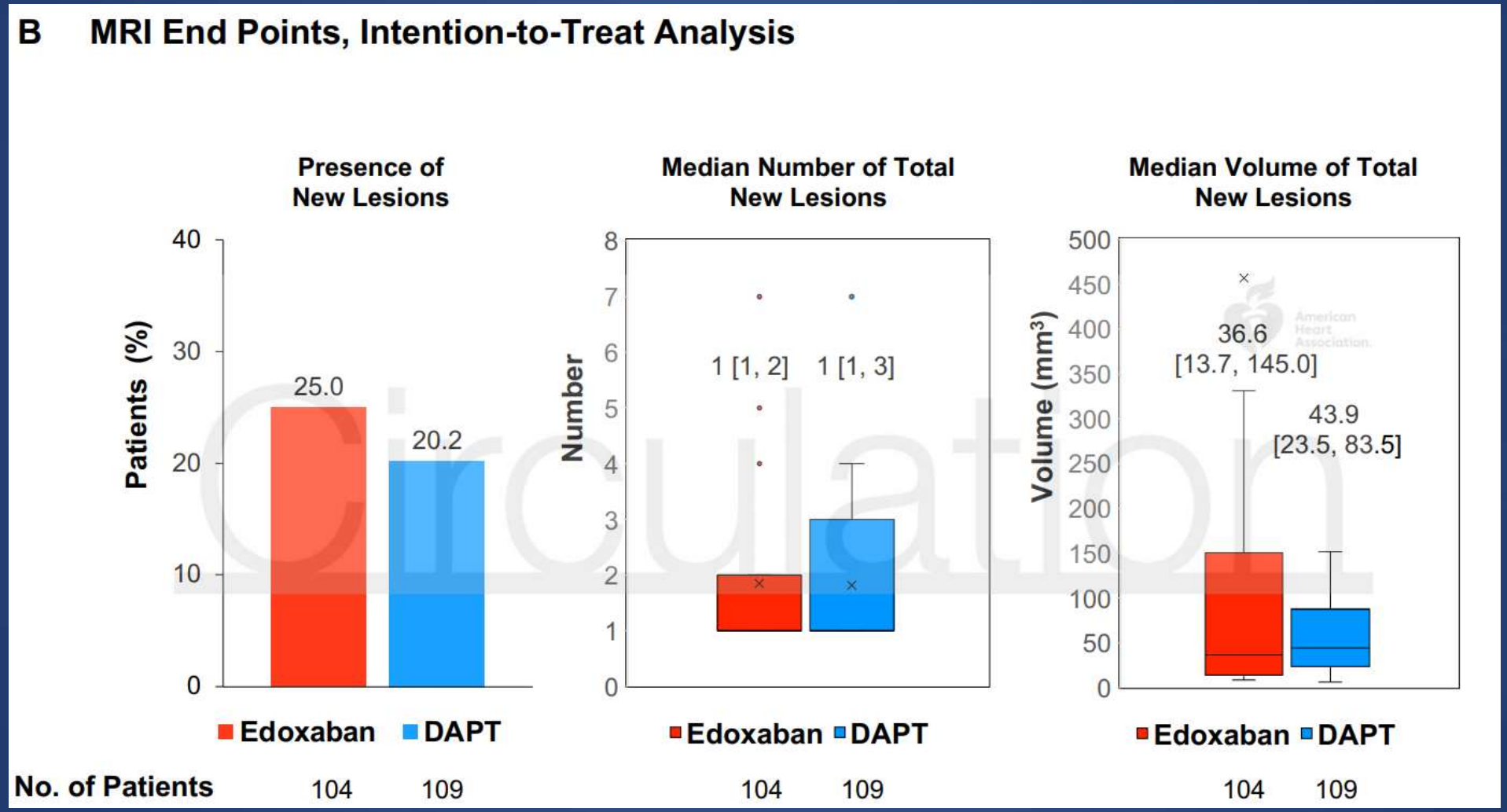
- All study subjects will undergo detailed neurologic and cognitive assessment at 1-7 days (baseline) and 6 months post-TAVR procedure

- Neurologic assessments included standard clinical scales (the National Institutes of Health Stroke Scale [NIHSS] and the modified Rankin Scale [mRS]), and cognitive assessments included the Montreal Cognitive Assessment (MoCA).

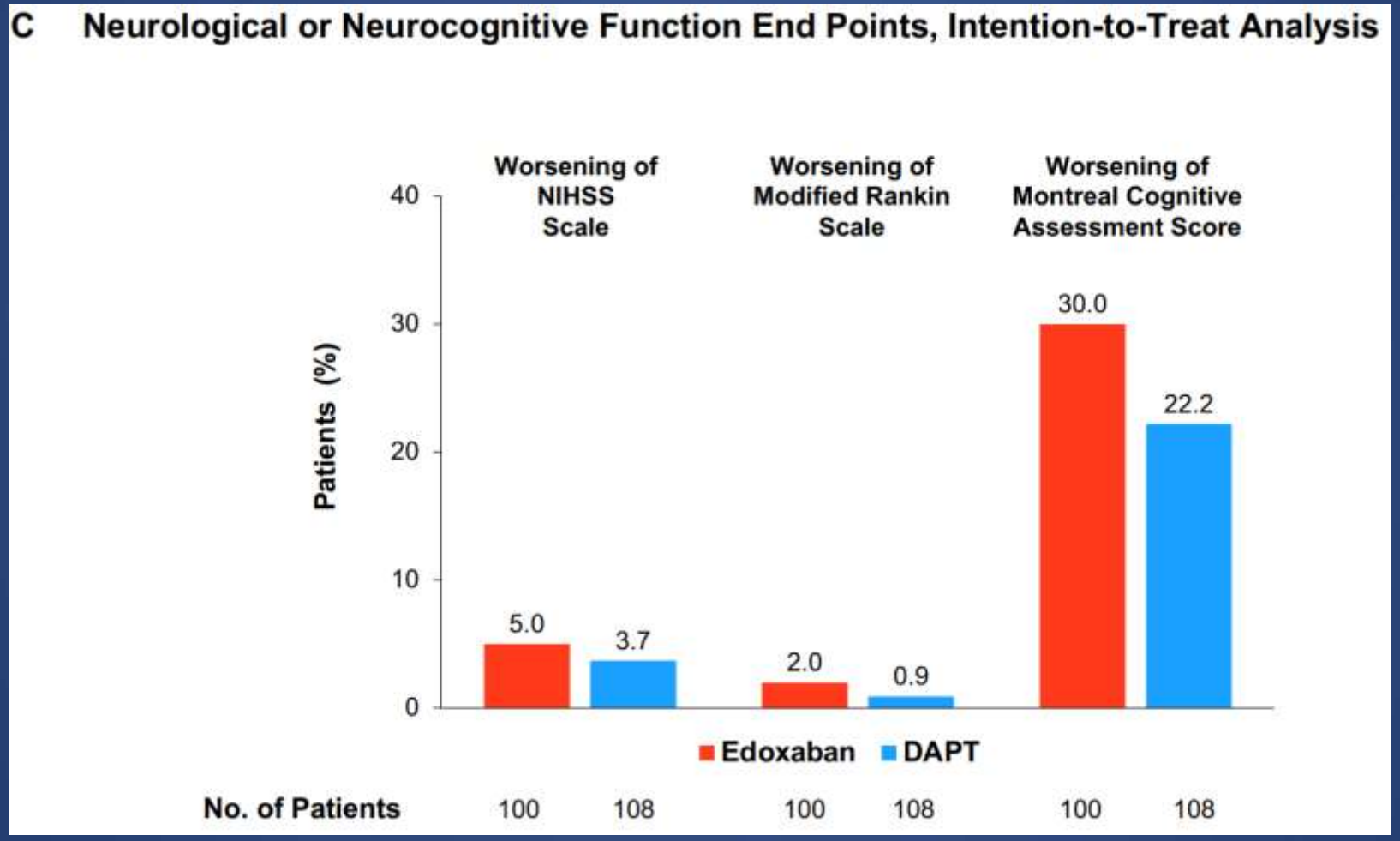
CT End Points



MRI End Points

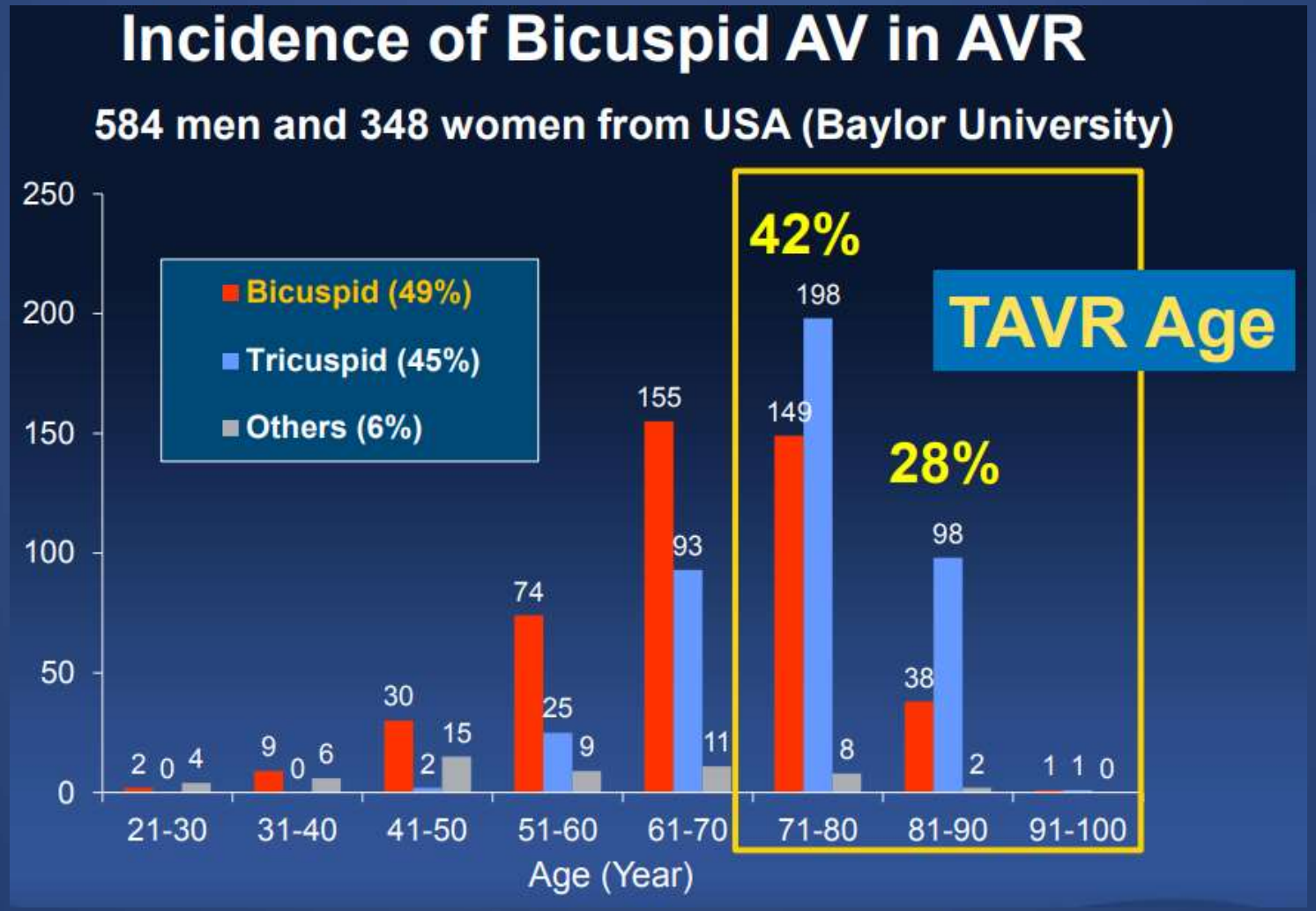


Neurological or Neurocognitive Function End Points



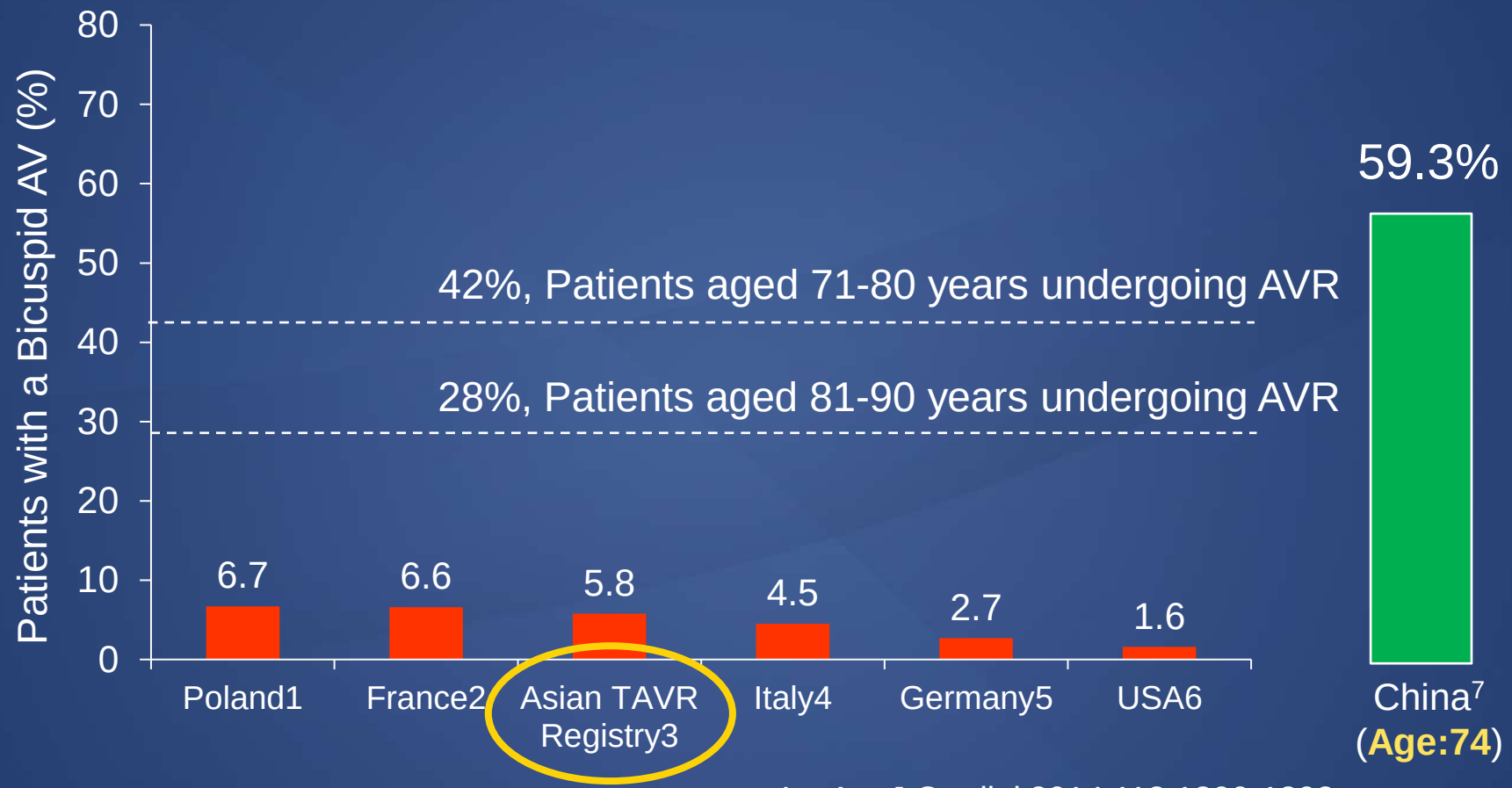
Bicuspid aortic valve

BAV burden in patients referred for TAVR



Roberts WC et al. Circulation 2005;111:920-925

Frequency of Bicuspid AV in TAVR registry



1. Am J Cardiol 2014;114:757-762
2. Am J Cardiol 2012;110:877-883
3. JACC Cardiovasc Interv 2016;9:926-33
4. Am J Cardiol 2014;113:1390-1393
5. Am J Cardiol 2014;113:518-521
6. JAMA 2013;310:2069-2077
7. Catheter Cardiovasc Interv. 2017;89(S1):528-533.

TAVR challenges in BAV

Anatomical

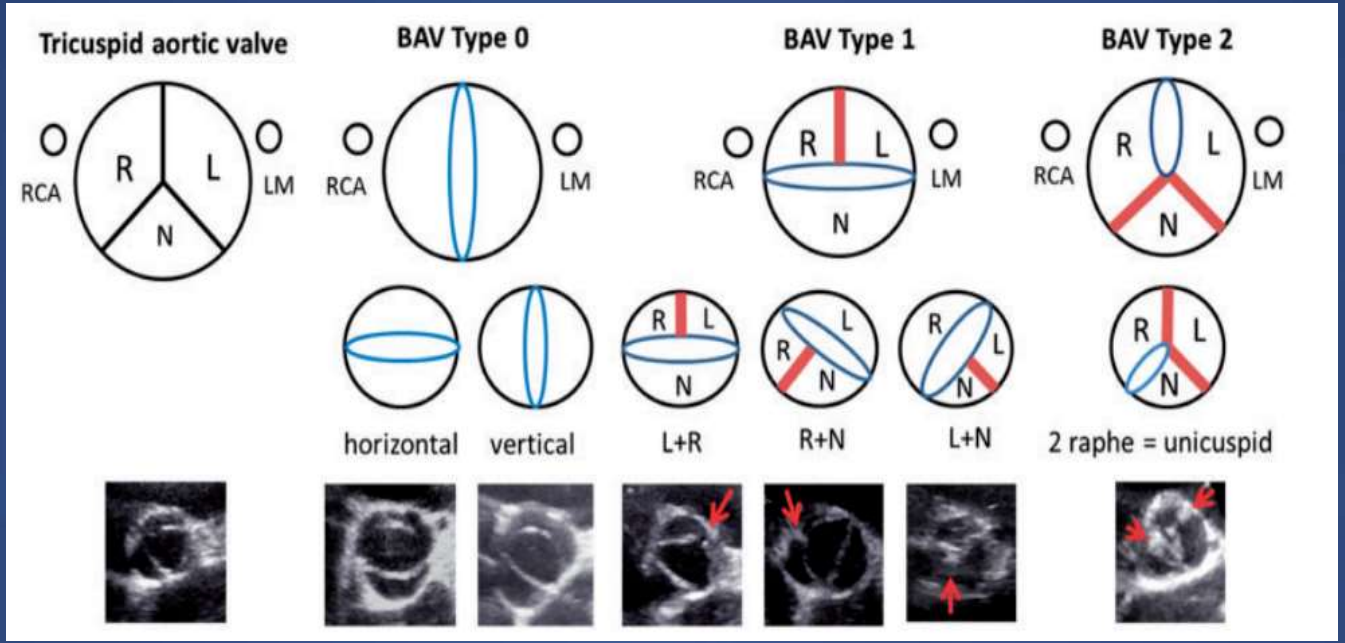
- Annular eccentricity
- Asymmetrical heavy valve calcification
- Unequally-sized leaflets
- Calcified raphe
- Concomitant aortopathy

Procedural

- Elliptical deployment
- Impaired Bioprosthesis Durability
- Residual Aortic Regurgitation
- Annulus Rupture
- Coronary Obstruction
- Aortic Complication

Zhao ZG et al. Nat. Rev. Cardiol 2015;12:123-128

Classification of BAV anatomy

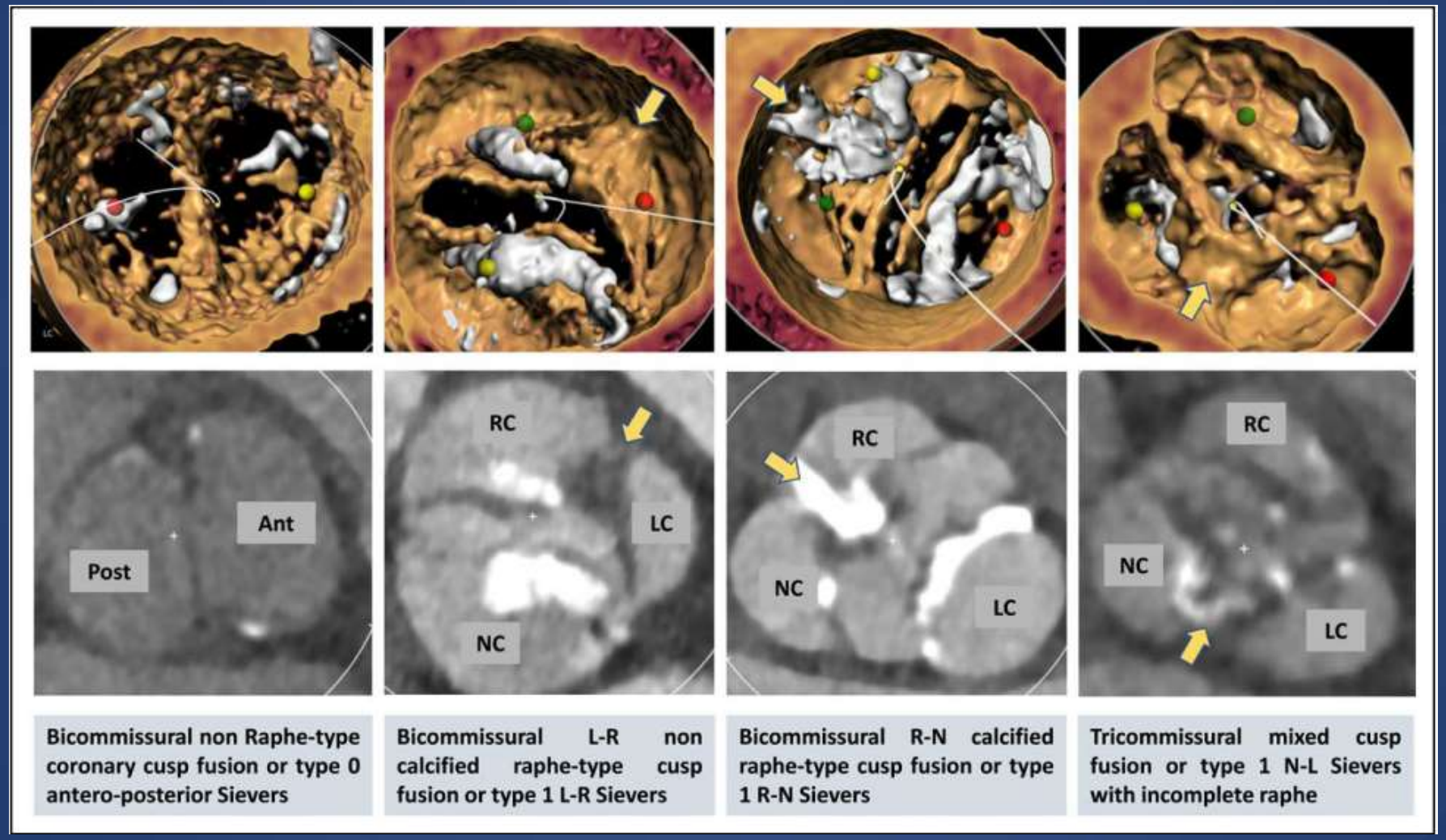


Inter-ethnic differences in BAV

	European (*n* = 794)	Asian (*n* = 633)
Morphology of BAV		
Type 0	115 (14.5)	43 (6.8)
Type 1 L+R	544 (68.5)	424 (67.0)
Type 1 R+N	108 (13.6)	125 (19.7)
Type 1 L+N	22 (2.8)	38 (6.0)
Type 2	5 (0.6)	3 (0.5)

WKF Kong et al. European Heart Journal 2018;39:1308–1313

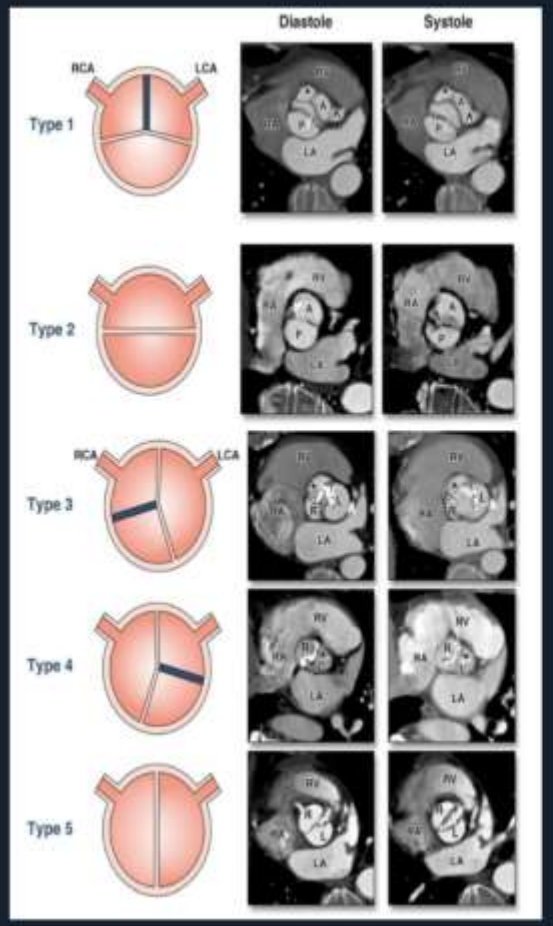
Classification of BAV anatomy



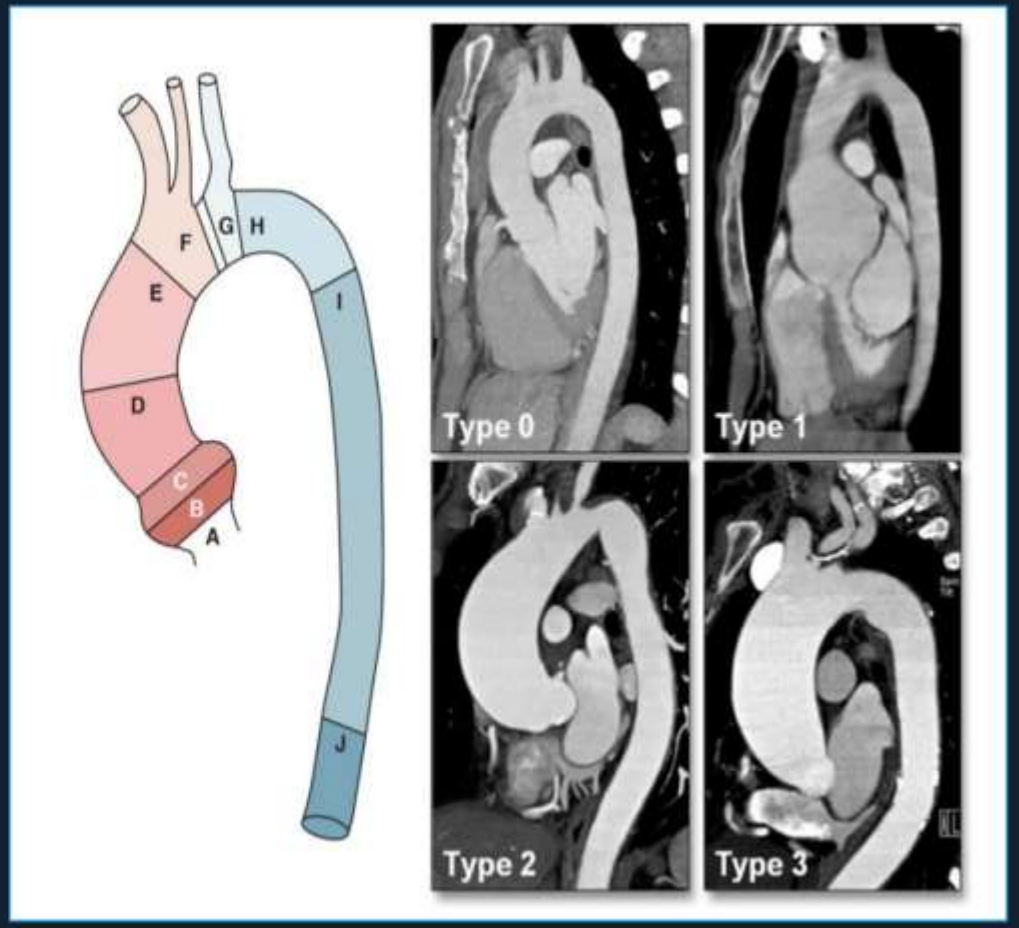
Flvien Vincent et al. Circulation 2021;143:1043-1061

Spectrum of BAV Disease

Aortic Valve Morphology

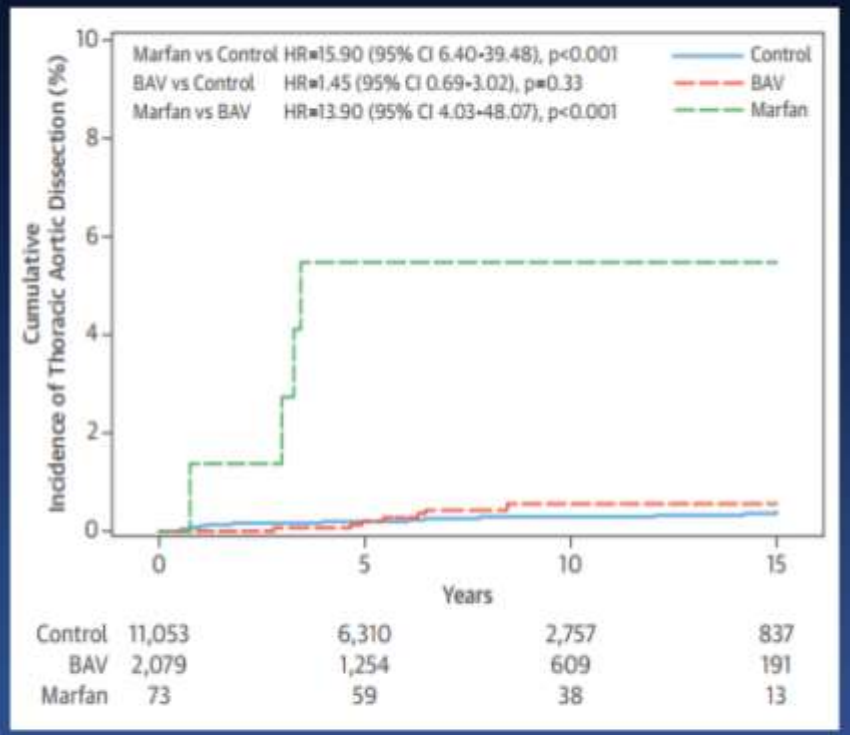


Combined Aortopathy



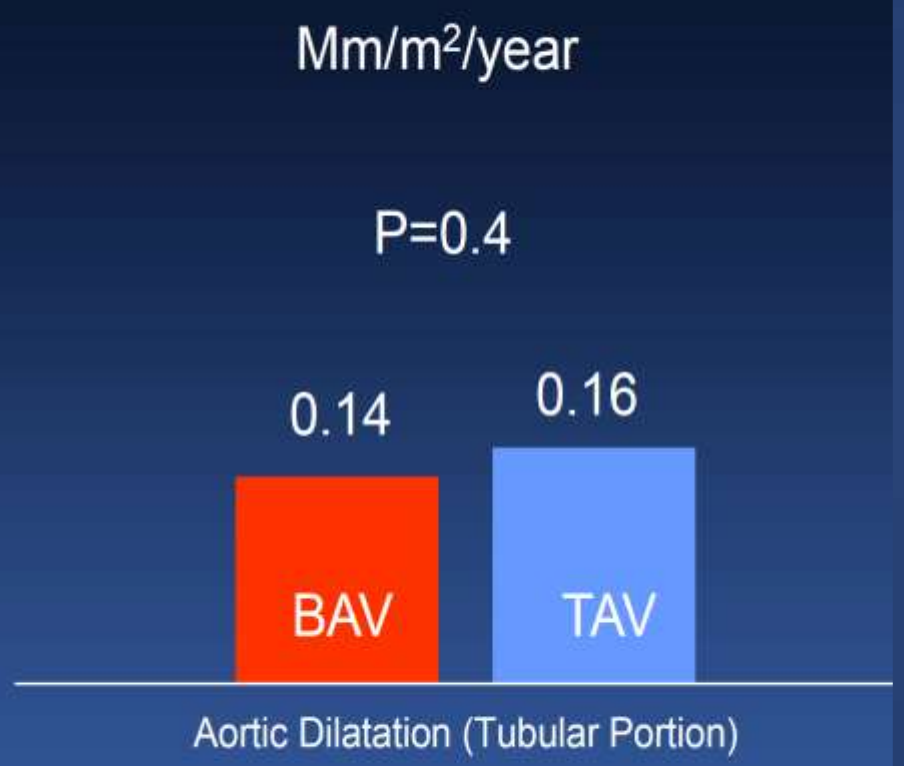
BAV Aortopathy

Risk Aortic Dissection After SAVR



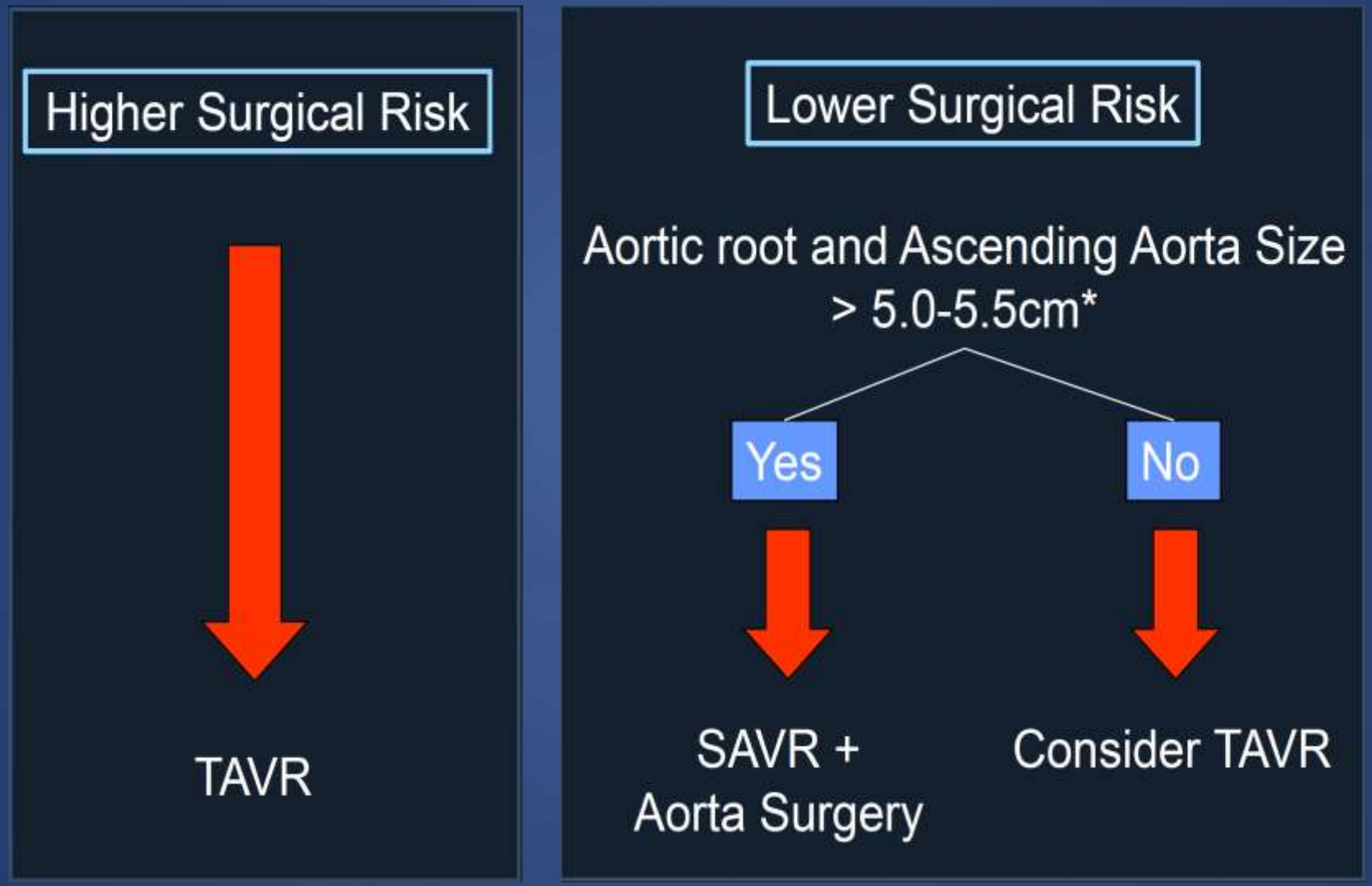
Itagaki S et al. JACC 2015 Jun 9;65(22):2363-9

Rate of Ao Dilatation After SAVR



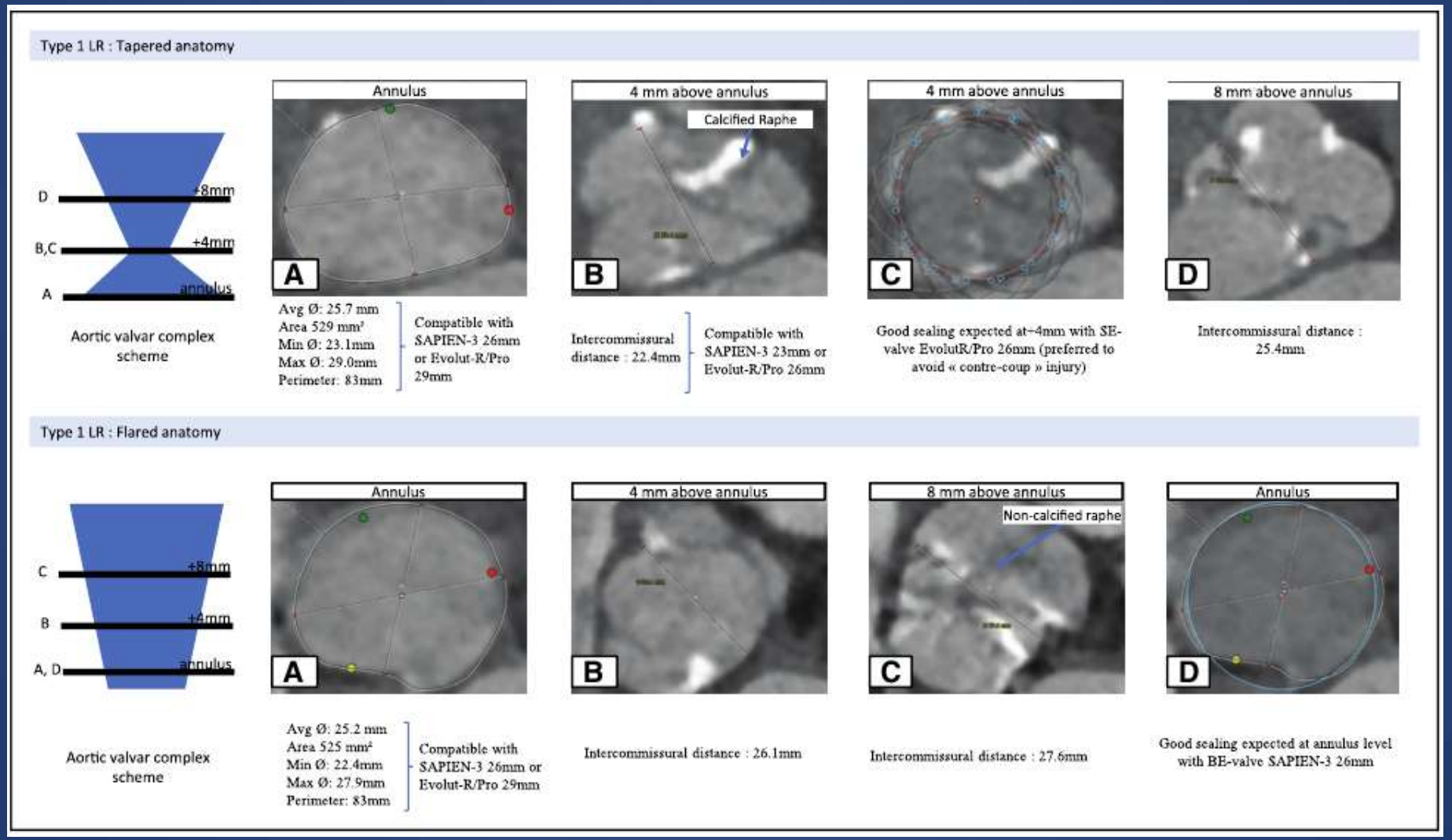
Kim YG et al. 2012 Dec;98(24):1822-7

BAV Aortopathy



JACC 2016 Surgery for Aortic Dilatation in Patients With Bicuspid Aortic Valves

CT sizing strategy and transcatheter valve design choice in BAV



Flvien Vincent et al. Circulation 2021;143:1043-1061

Outcomes of observational study of TAVR in BAV patients

	Bauer (N=38)	Kochman (N=28)	Yousef (N=108)	Mylotte (N=139)	Jilaihawi (N=130)
Age, years	81	78	76	78	77
Mean STS score (%)	-	-	-	4.9	4.7
Type of Valve (%)					
Balloon Expandable	32	18	56	28	54
Self Expandable	68	82	44	72	46
New Pacemaker (%)	17	29	19	23	26
PVL>mild (%)	25	32	31	28	18
30-day Stroke (%)	0	0	2.8	2.2	3.2
30-day Survival (%)	89	96	92	95	96

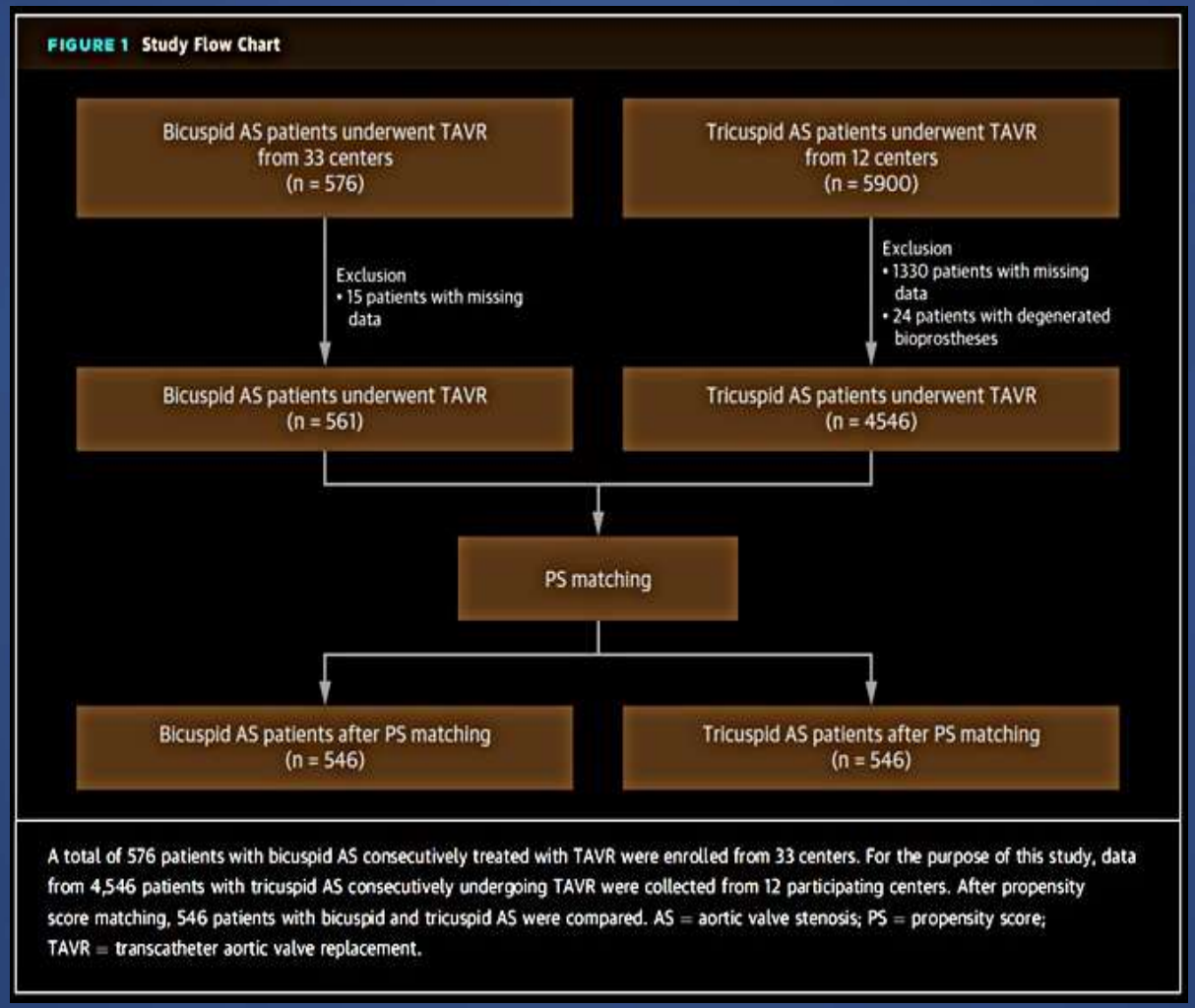
Bauer T et al. Am J Cardiol. 2014 ;113:518-21
Kochman et al. Am J Cardiol. 2014;114:757-62
Yousef et al. Int J Cardiol 2015;189:282-8
Mylotte al. J Am Coll Cardiol 2014 ;64:2330
Jilaihawi et al. JACC:Cardiovascular Imaging 2016;9:1145-58

Outcomes of observational study of TAVR in BAV patients

	Liao (N=87)	Elbadawi (N=1055)	Makkar (N=2726)	Halim (N=5412)	Forrest (N=932)	Yoon (N=1034)
Age, years	73	68	73	74	73	75
Mean STS score (%)	7.9	-	4.9	3.8	5.3	3.7
Type of Valve (%)		-				
Ballon Expandable	0	-	100	81	0	72
Self Expandable	100	-	0	19	100	24
New Pacemaker (%)	24	14	9	-	15	12.2
PVL>mild (%)	14	-	2	4	6	3.4
Stroke (%)	1.1	1.9	2.5	2.2	3.4	2.7
30-day Survival (%)	90.8	97.1	97.4	98	97.4	98

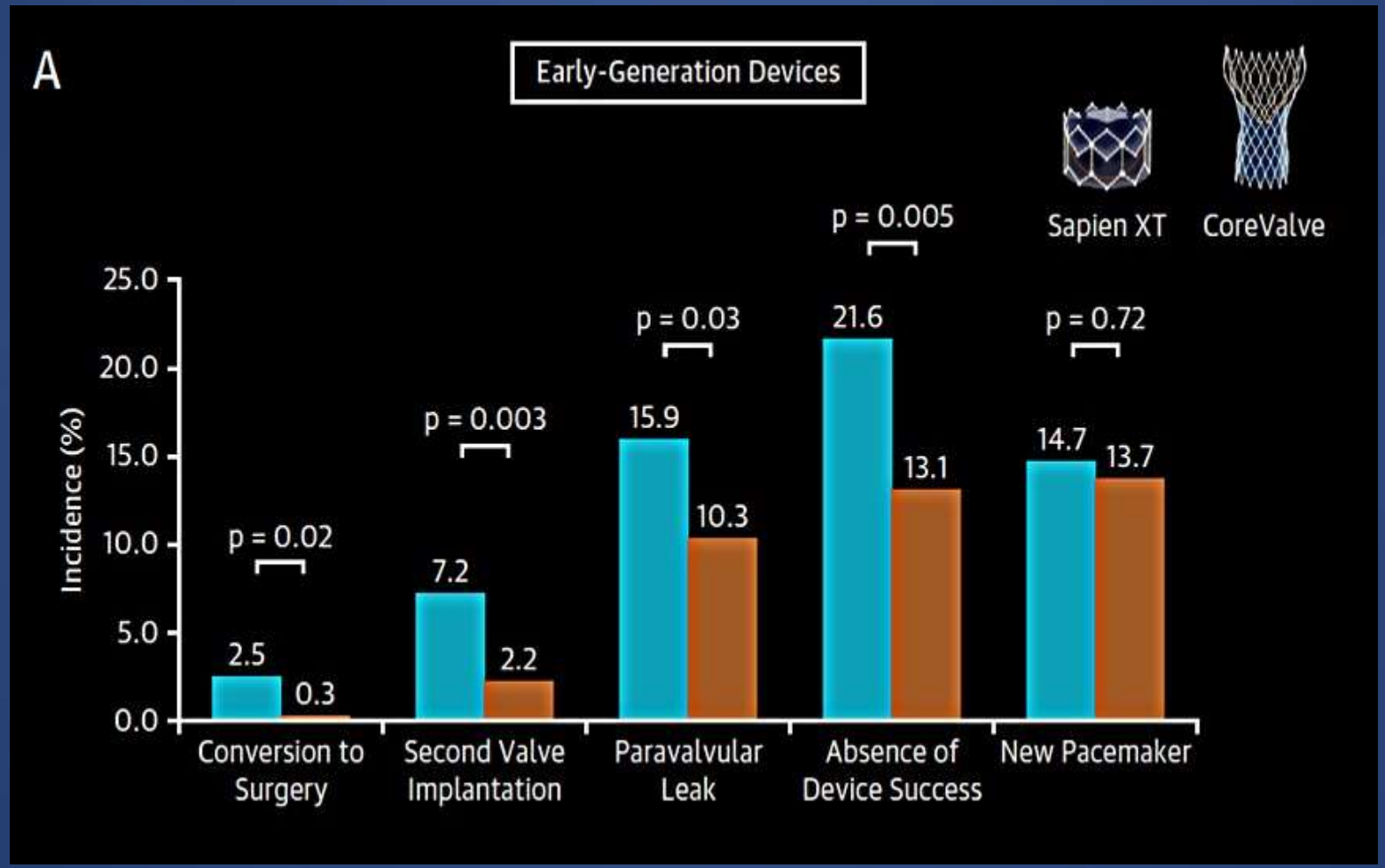
Liao et al. Int J Cardiology 2018;254:69-74
Elbadawi et al. JACC Cardiovasc interv.2019;12:1811-1822
Makkar et al. JAMA 2019;321:2193-2202
Halim et al. Circulation 2020;141:1071-1079
Forrest et al. JACC Cardiovasc interv.2020;13:1749-1759
Yoon et al. J Am Coll Cardiol 2020;76:1018-1030

2-year outcomes of Bicuspid vs. Tricuspid with PS matching



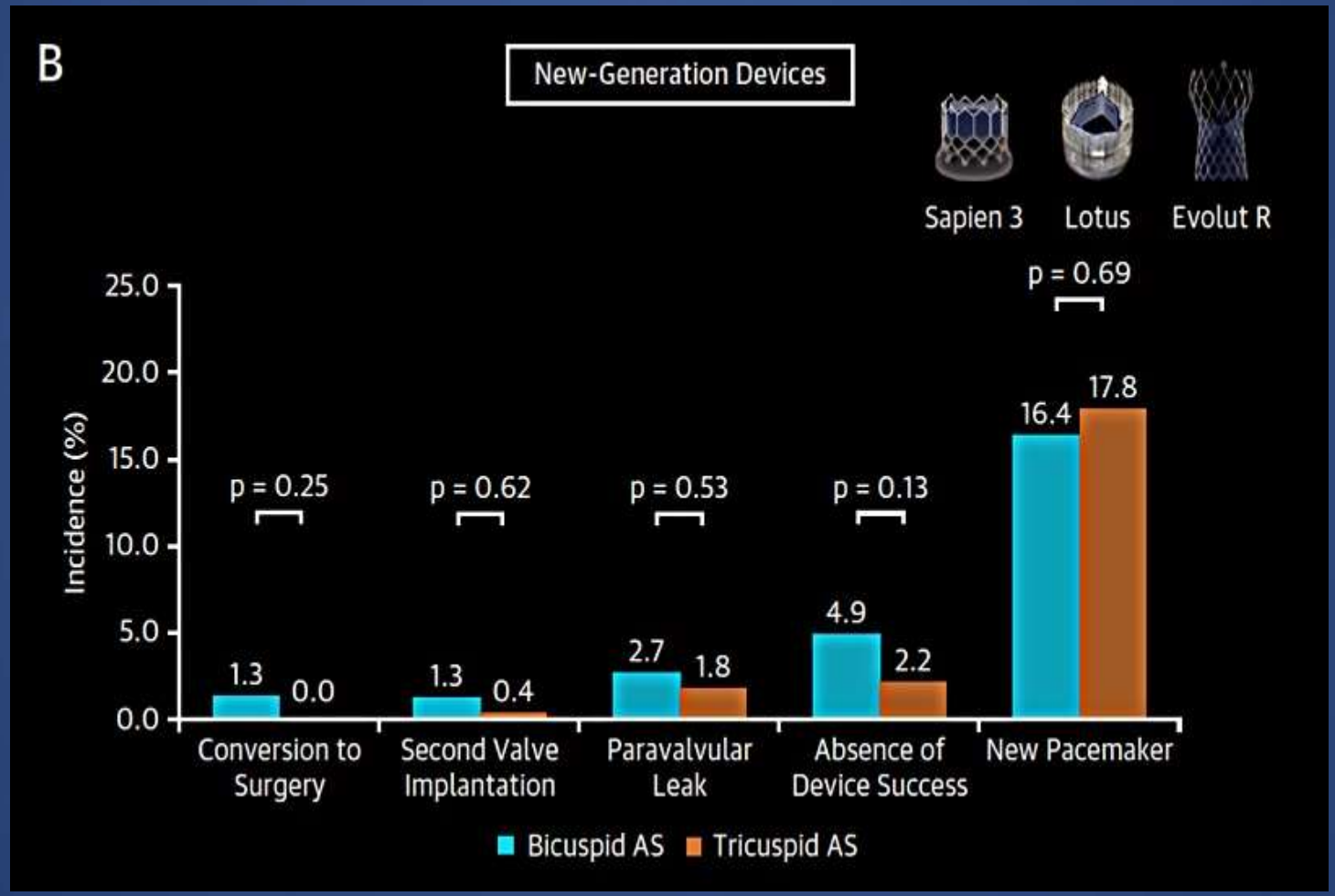
SH Yoon et al. JACC 2017;69:2579-89

2-year outcomes of Bicuspid vs. Tricuspid with PS matching



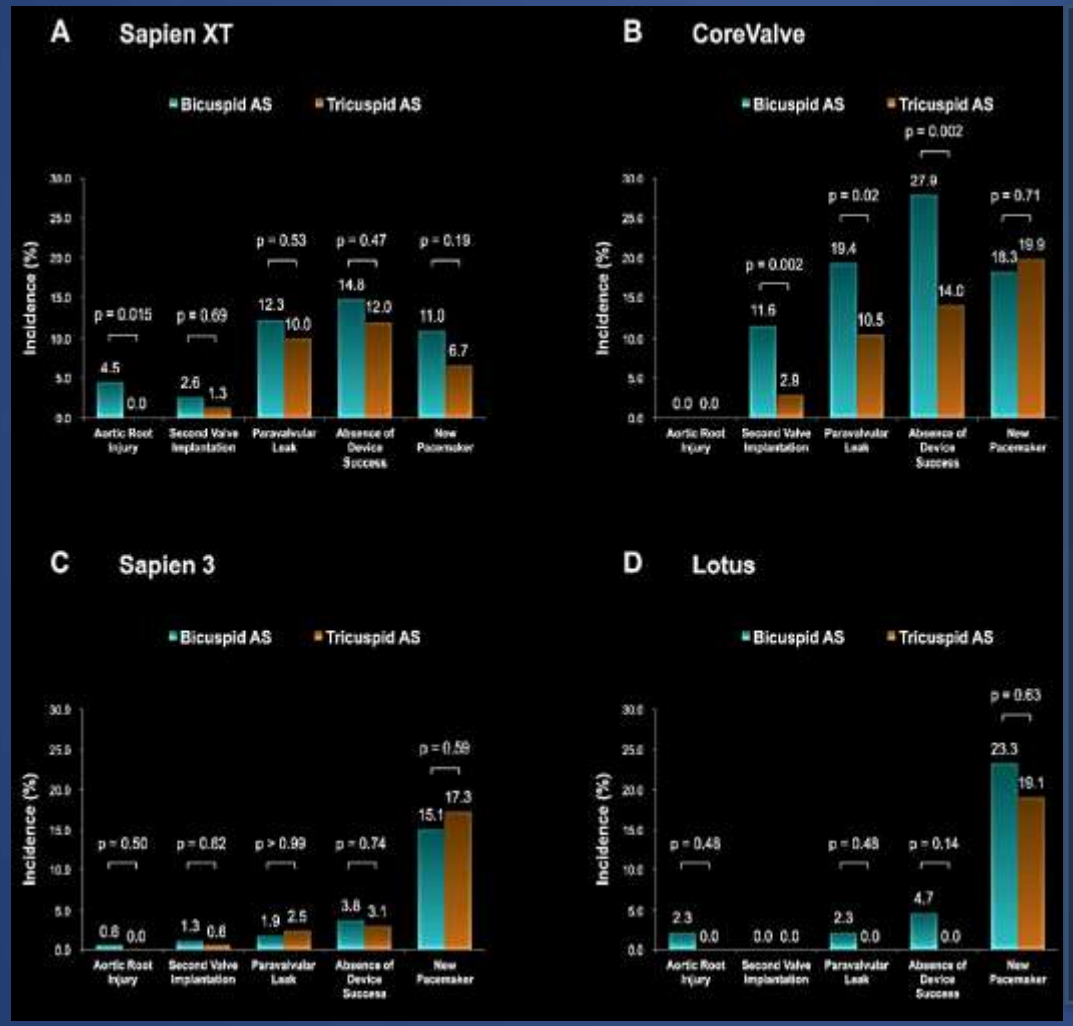
SH Yoon et al. JACC 2017;69:2579-89

2-year outcomes of Bicuspid vs. Tricuspid with PS matching



SH Yoon et al. JACC 2017;69:2579-89

Procedural and Clinical Outcomes in Transcatheter Aortic Valve Replacement for Bicuspid Versus Tricuspid Aortic Valve Stenosis

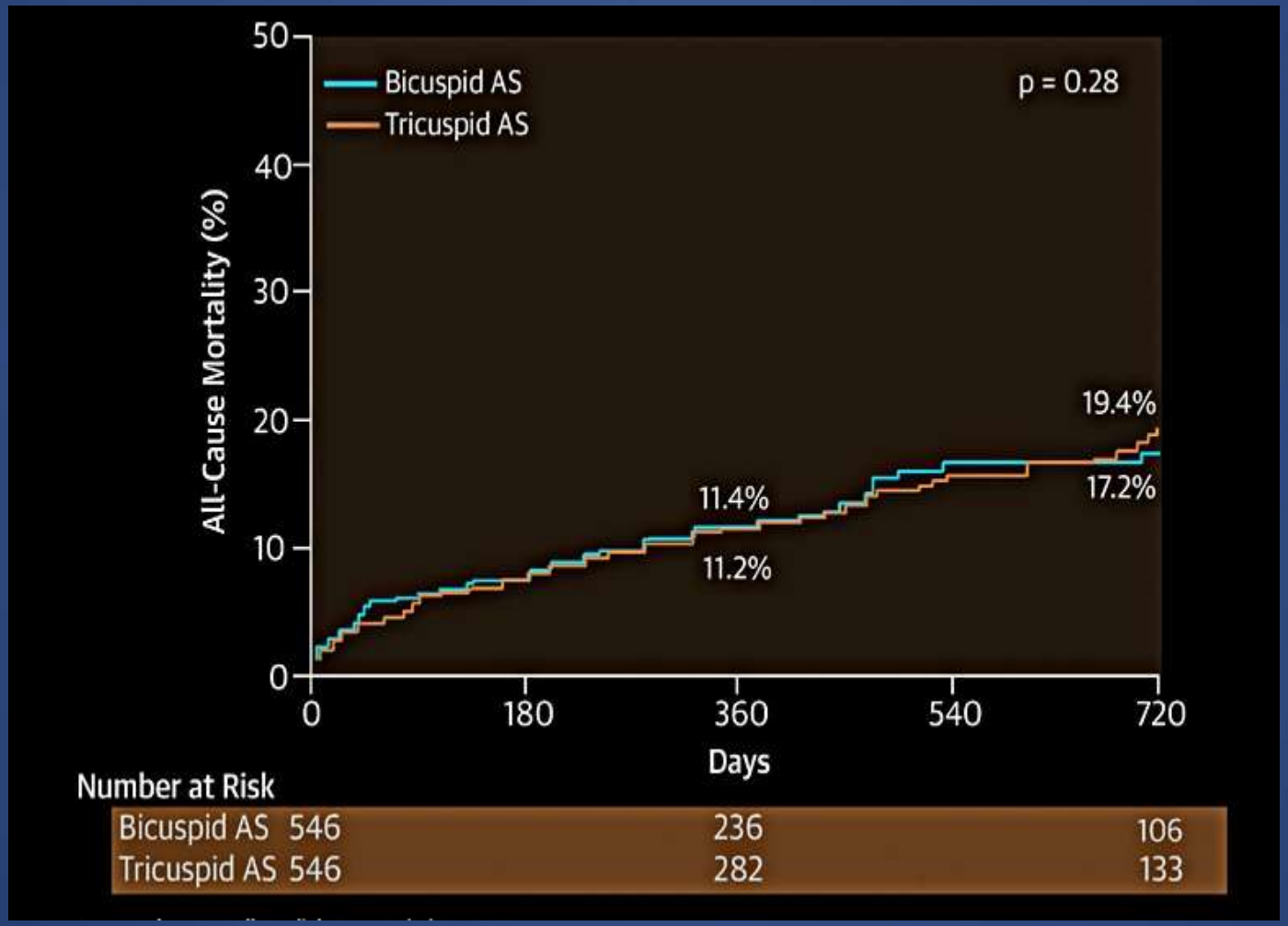


Within the group receiving early generation devices, bicuspid AS had more frequent

- aortic root injury when receiving the Sapien XT (4.5% vs. 0.0%; p=0.015)
- Moderate to severe PVL when receiving the CoreValve (19.4% vs. 10.5%; p=0.02)
- Among patients with new generation devices, procedural results were comparable across different prostheses.

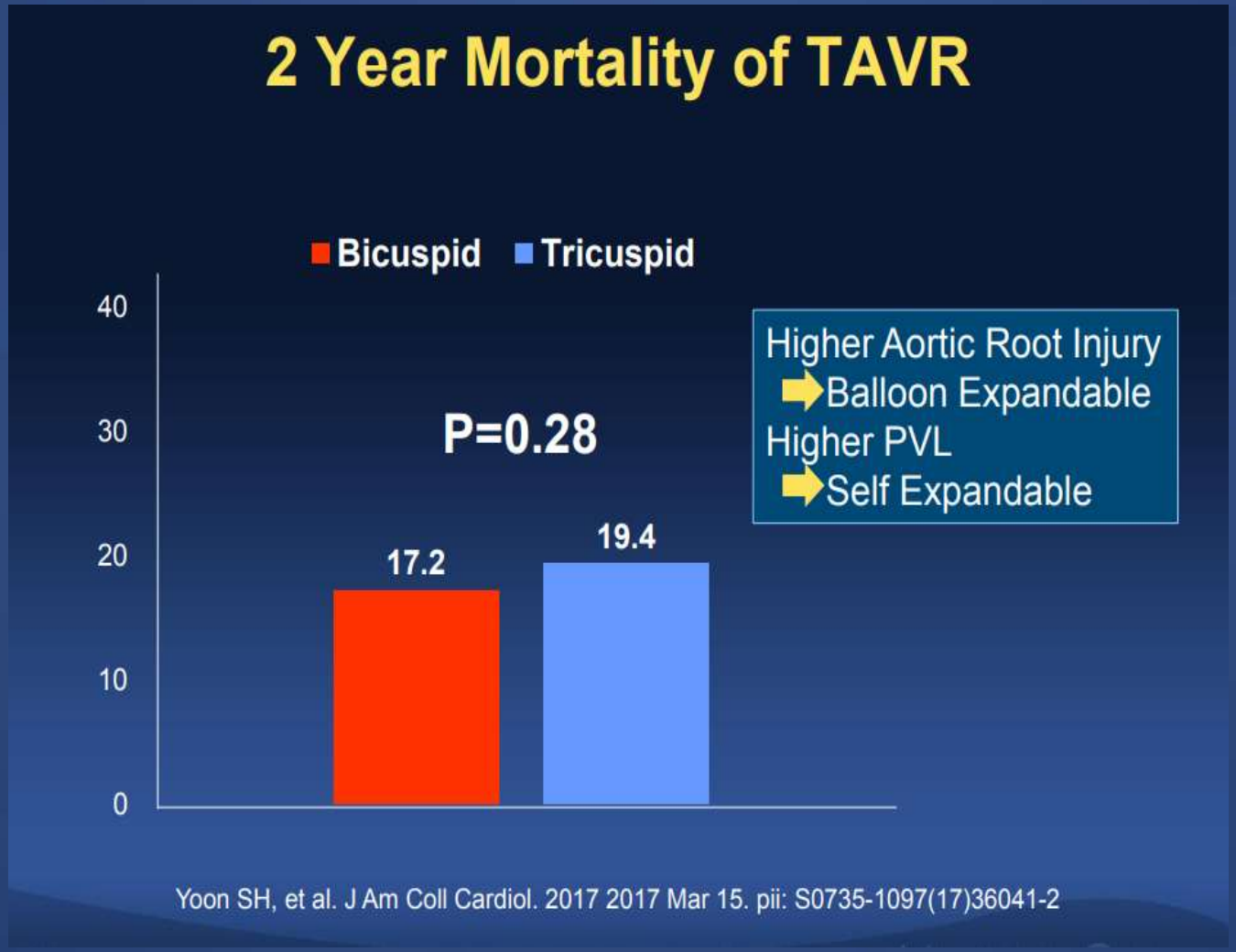
Yoon SH, et al. J Am Coll Cardiol. 2017 Mar 15. [Epub ahead of print]

2-year outcomes of Bicuspid vs. Tricuspid

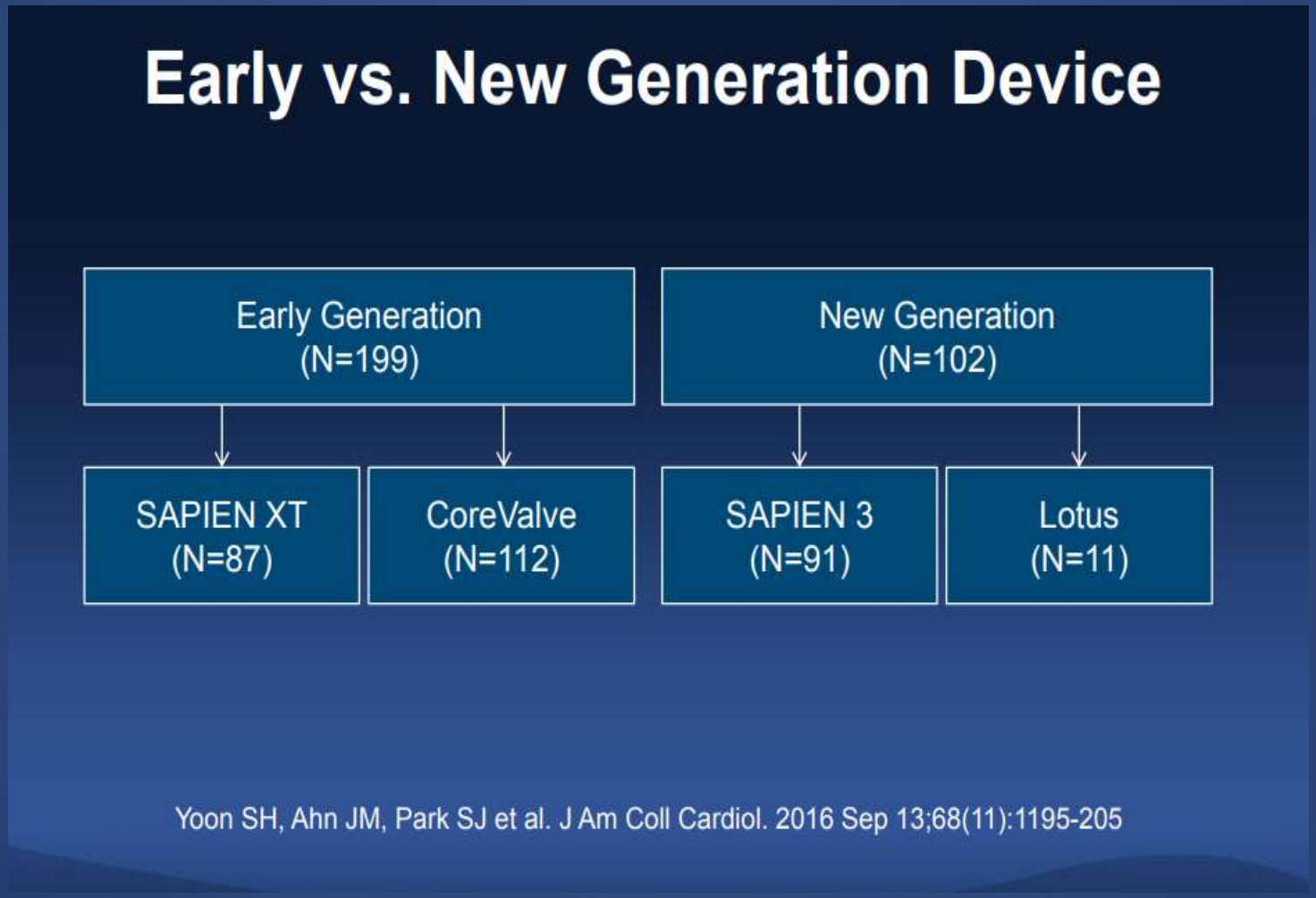


SH Yoon et al. JACC 2017;69:2579-89

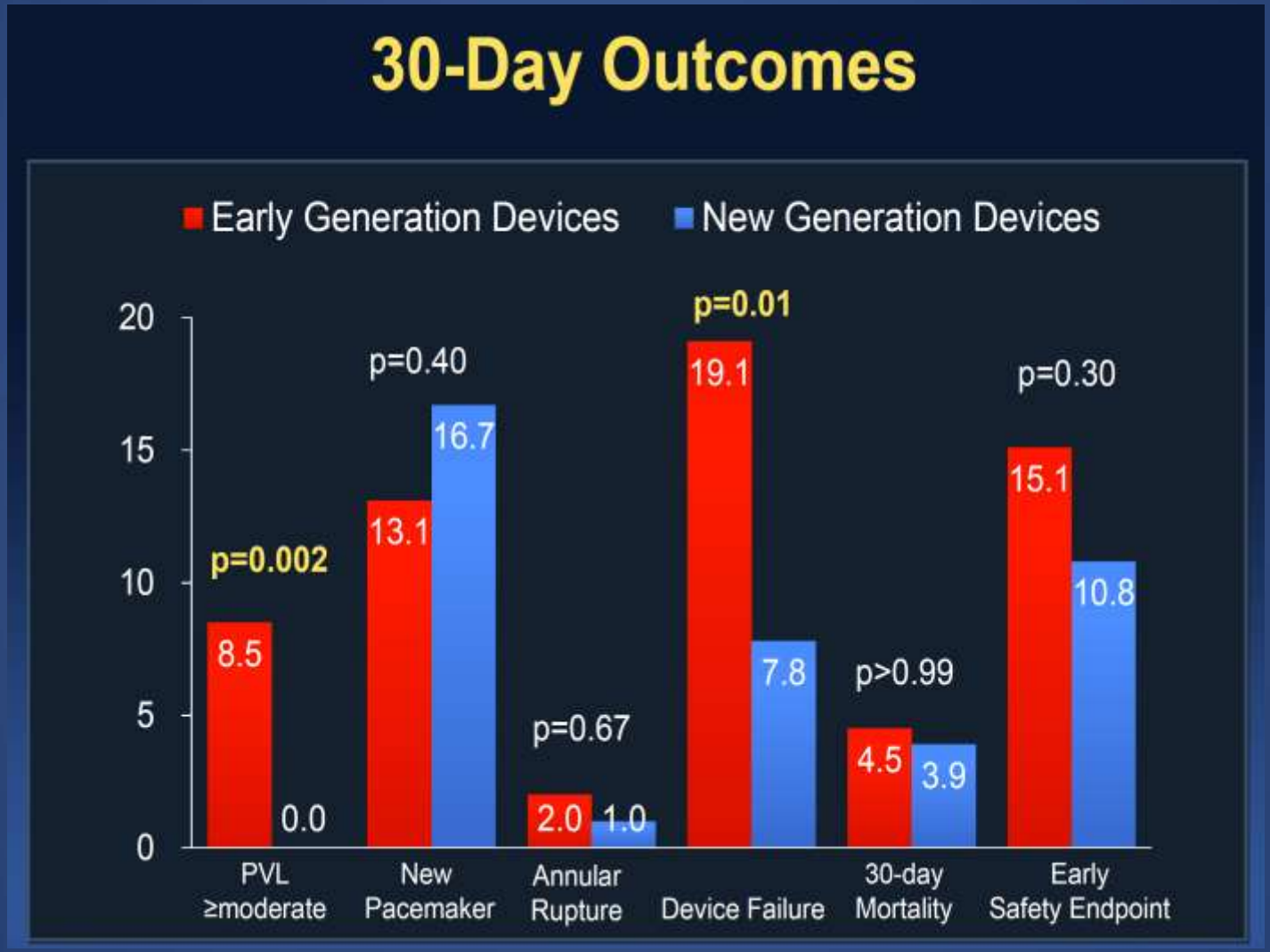
2-year outcomes of Bicuspid vs. Tricuspid with PS matching



Bicuspid TAVR in Asians

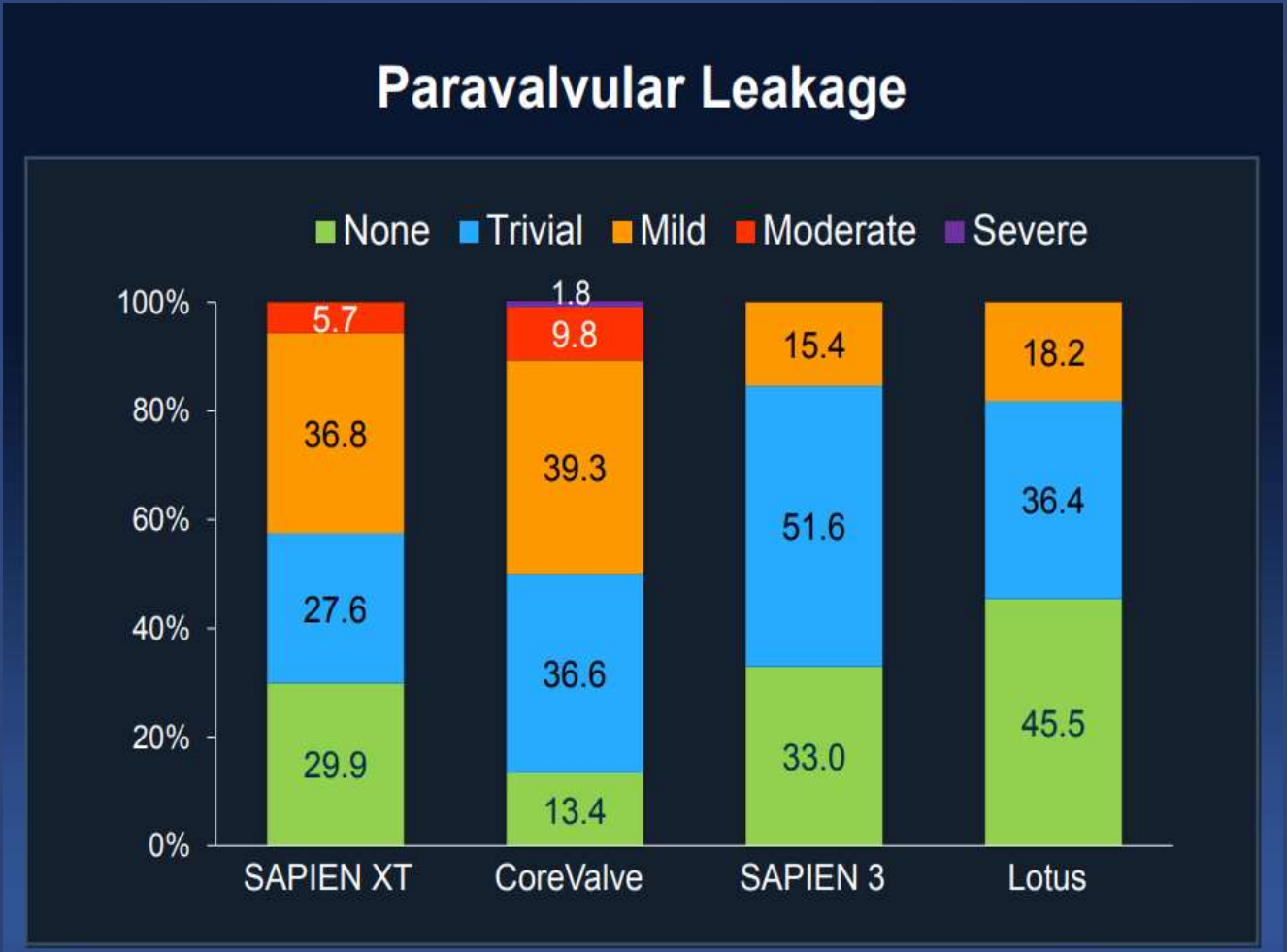


Bicuspid TAVR in Asians



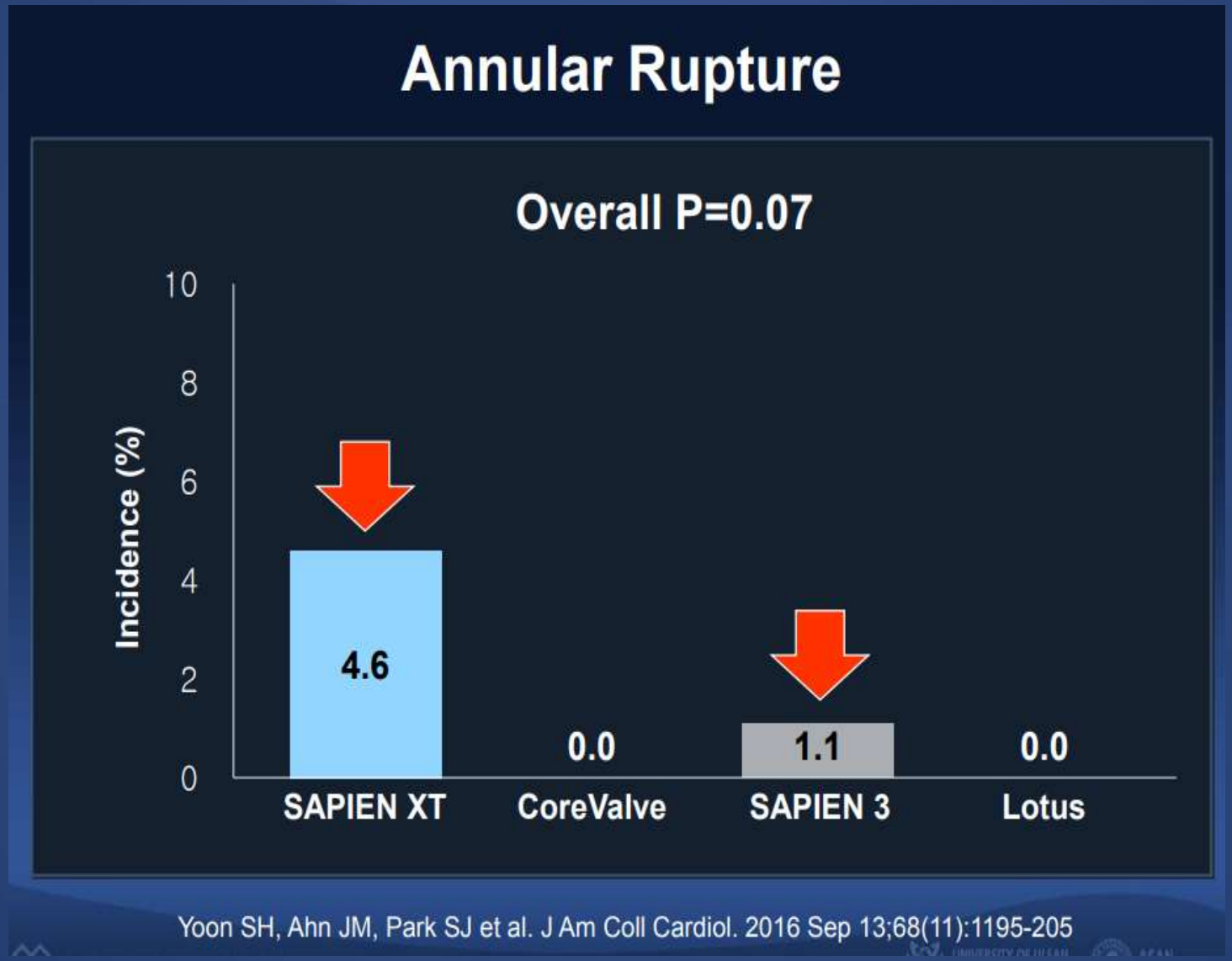
Yoon SH, Ahn JM, Park SJ et al. JACC 2016;68(11):1195-20

Bicuspid TAVR in Asians



Yoon SH, Ahn JM, Park SJ et al. J Am Coll Cardiol. 2016 Sep 13;68(11):1195-205

Bicuspid TAVR in Asians



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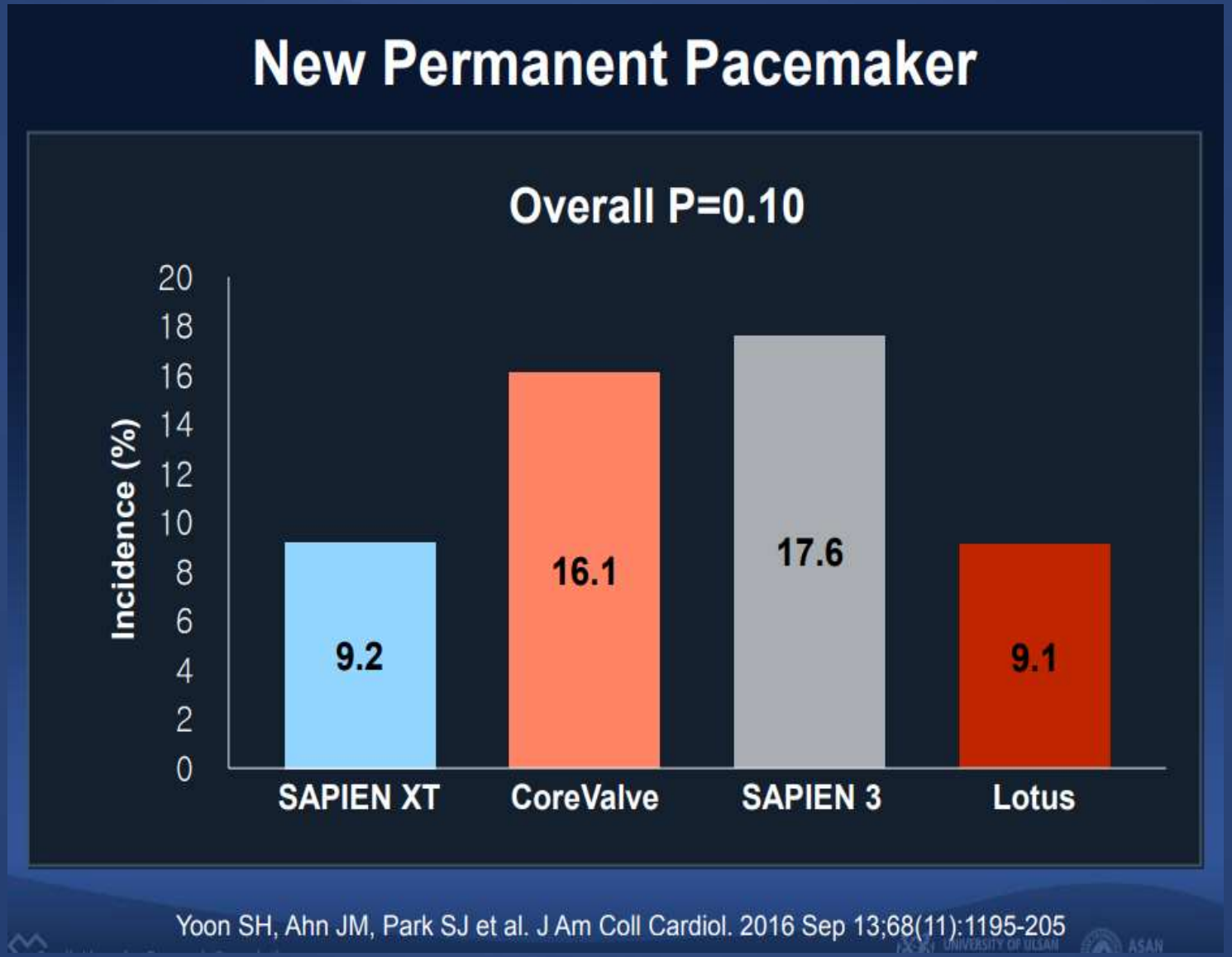
Bicuspid TAVR in Asians



Yoon SH, Ahn JM, Park SJ et al. J Am Coll Cardiol. 2016 Sep 13;68(11):1195-205

Outcomes of TAVR with Sapien3 Valve in Bicuspid Aortic Stenosis:

An analysis of the STS/ACC TVT Registry

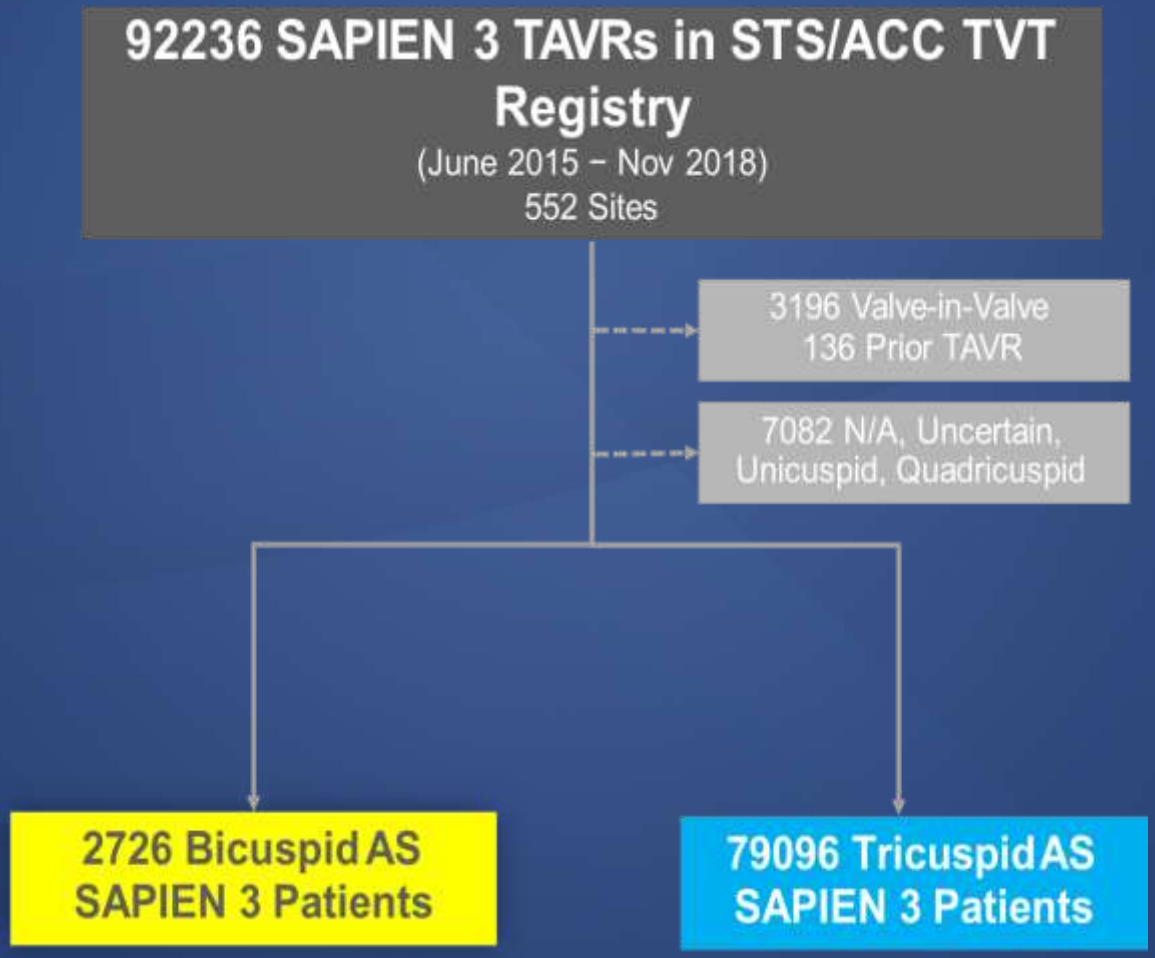
STS/ACC TVT Registry
Background & Objective

- Bicuspid aortic valve accounts for up to 50% of patients requiring surgical aortic valve replacement in the younger population[1]
- As TAVR becomes a therapeutic option for younger and healthier patients, bicuspid aortic valves will be seen more often.
- Pivotal clinical trials, including the low risk trials enrolling younger patients, have excluded patients with bicuspid aortic valves.
- We sought to compare the outcomes of TAVR with balloon-expandable SAPIEN 3 valve in native bicuspid versus tricuspid aortic valve stenosis in the real-world ST S/ACC TVT Registry.

[1]Roberts WC, Ko JM. Circulation. 2005;111(7):920-925

STS/ACC TVT Registry

Study Population



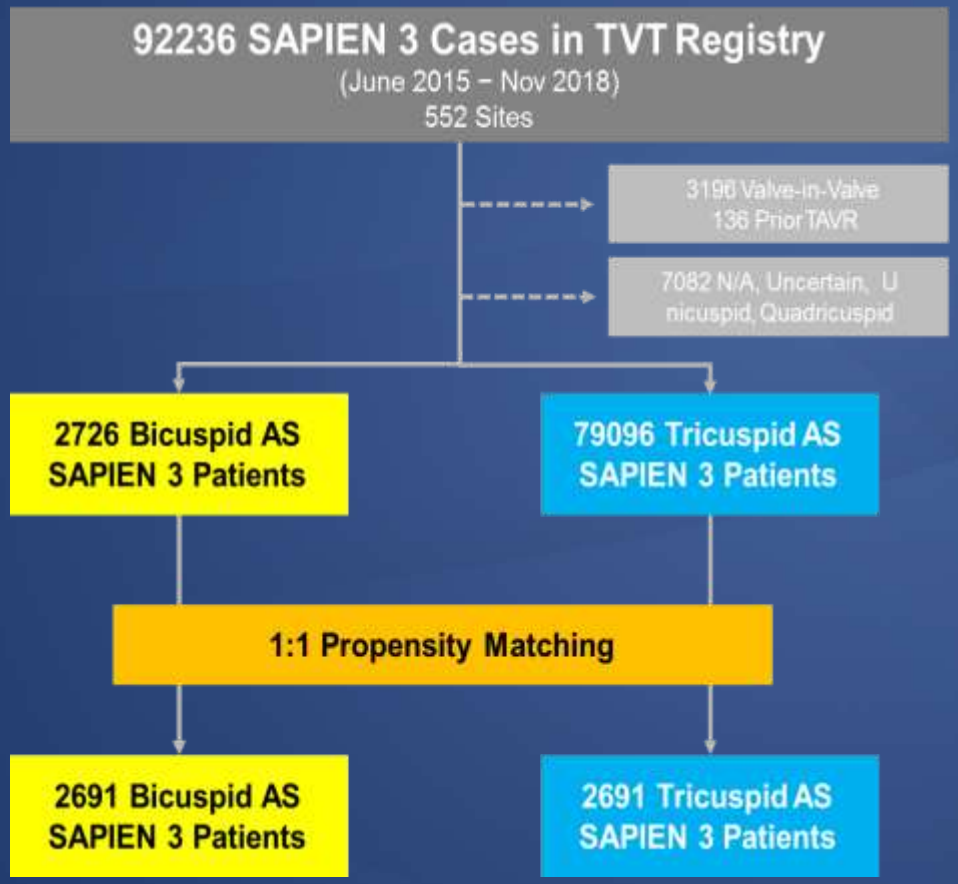
STS/ACC TVT Registry

Baseline Characteristics – Unadjusted

Characteristic % or mean ± SD	Bicuspid AS (n=2726)	Tricuspid AS (n=79096)	p-value
Age (years)	**72.8 ± 10.74**	**80.8 ± 8.10**	**<0.0001**
STS Risk Score (%)	**4.9 ± 3.96**	**6.5 ± 4.60**	**<0.0001**
Male	60.4	55.1	<0.0001
NYHA III/IV	74.3	75.4	0.2
BMI (kg/m^2)	29.2 ± 7.64	29.0 ± 7.25	0.13
Hypertension	84.1	91.2	<0.0001
Diabetes	35.7	38.8	0.001
Peripheral Arterial Disease	24.1	27.6	<0.0001
Carotid Stenosis	**14.8**	**25.2**	**<0.0001**
Atrial Fibrillation	**28.8**	**38.7**	**<0.0001**
Prior Stroke	10.2	11.5	0.04
Chronic Lung Disease	41.5	40.1	0.13
Prior PCI	25.2	34.0	<0.0001
Prior CABG	**15.7**	**20.8**	**<0.0001**
Porcelain Aorta	2.7	3.4	0.052
GFR (mL/min/1.73 m^2)	**65.3 ± 28.69**	**59.3 ± 24.45**	**<0.0001**
5MWT (seconds)	7.5 ± 4.16	8.4 ± 5.44	<0.0001

STS/ACC TVT Registry

Study population



25 Covariates used for propensity matching	
Age	Chronic Lung Disease
Gender (male)	Prior PCI
NYHA III/IV	Prior CABG
BMI	Porcelain Aorta
Hypertension	Mean Gradient
Diabetes	LVEF
Creatinine ≥ 2	Mitral Regurgitation
Peripheral Arterial Disease	Tricuspid Regurgitation
Carotid Stenosis	5 Meter Walk Test
Atrial Fibrillation	Access Site
Prior Stroke	KCCQ
Immunocompromised	Hemoglobin
GFR	

STS/ACC TVT Registry

Baseline Characteristics – Matched

Characteristic % or mean ± SD	Bicuspid AS (n=2691)	Tricuspid AS (n=2691)	p-value
Age (years)	73.1 ± 10.46	72.9 ± 10.95	**0.47**
STS Risk Score (%)	4.9 ± 3.96	5.1 ± 4.18	**0.09**
Male	60.3	61.5	**0.35**
NYHA III/IV	74.4	74.1	**0.83**
BMI (kg/m^2)	29.2 ± 7.62	29.4 ± 7.40	**0.30**
Hypertension	84.5	84.2	**0.80**
Diabetes	35.8	36.8	**0.43**
Peripheral Arterial Disease	24.3	24.5	**0.90**
Carotid Stenosis	15.0	15.6	**0.63**
Atrial Fibrillation	29.0	29.4	**0.73**
Prior Stroke	10.2	10.2	**0.96**
Chronic Lung Disease	41.7	42.0	**0.79**
Prior PCI	25.5	26.6	**0.34**
Prior CABG	15.9	17.2	**0.18**
Porcelain Aorta	2.7	3.1	**0.37**
GFR ($mL/min/1.73\,m^2$)	65.0 ± 28.42	64.4 ± 27.15	**0.39**
5MWT (seconds)	7.6 ± 4.17	7.6 ± 3.91	**0.79**

STS/ACC TVT Registry
Methods

- **Primary end-point:** Mortality and Stroke at 30-days and 1-year.

- **Secondary end-point:** Procedural complications, in-hospital adverse events, post-procedural echocardiographic assessment of the valve, functional status and health status at 30 days and 1 year.

- To compare death and stroke between bicuspid and tricuspid cohorts, the patients in the study cohort were linked with Centers for Medicare and Medicaid Services (CMS) claims data, in addition to the follow-up obtained from the TVT registry.

STS/ACC TVT Registry

Baseline Echo

Characteristic % or mean ± SD	Bicuspid AS (n=2691)	Tricuspid AS (n=2691)	p-value
AV Mean Gradient (mmHg)	45.2 ± 14.99	44.9 ± 15.20	0.51
AV Area (cm^2)	0.705 ± 0.2295	0.714 ± 0.2119	0.15
LVEF (%)	53.5 ± 14.73	52.5 ± 14.95	0.02
Annular Size (mm)	**25.076 ± 3.1969**	**24.632 ± 3.0372**	**<0.0001**
Mitral Regurgitation (mod/sev) (%)	20.6	21.7	0.39
Tricuspid Regurgitation (mod/sev) (%)	14.0	14.1	0.86

STS/ACC TVT Registry
Procedural Data

Characteristic %	Bicuspid AS (n=2691)	Tricuspid AS (n=2691)	p-value
Transfemoral access	93.6	93.9	0.65
Conscious Sedation	42.8	44.1	0.33
Valve Size			<0.0001
20mm	2.7	3.1	0.33
23mm	**23.0**	**28.5**	**<0.0001**
26mm	**39.1**	**42.0**	**0.03**
29mm	**35.2**	**26.4**	**<0.0001**

STS/ACC TVT Registry

Procedural Outcomes

Characteristic % or mean ± SD	Bicuspid AS (n=2691)	Tricuspid AS (n=2691)	p-value
Device success	96.5	96.6	0.87
Procedure Time, min	100.7 ± 51.80	98.2 ± 52.09	0.08
Fluoroscopy Time, min	18.5 ± 10.96	17.1 ± 10.17	<0.0001
Conversion to open surgery	**0.9**	**0.4**	**0.03**
Annulus Rupture	**0.3**	**0.0**	**0.02**
Cardiopulmonary bypass	1.4	1.0	0.13
Aortic dissection	0.3	0.1	0.34
Coronary Obstruction	0.4	0.3	0.34
Need for a second valve	**0.4**	**0.2**	**0.16**

STS/ACC TVT Registry

30-Day Outcomes

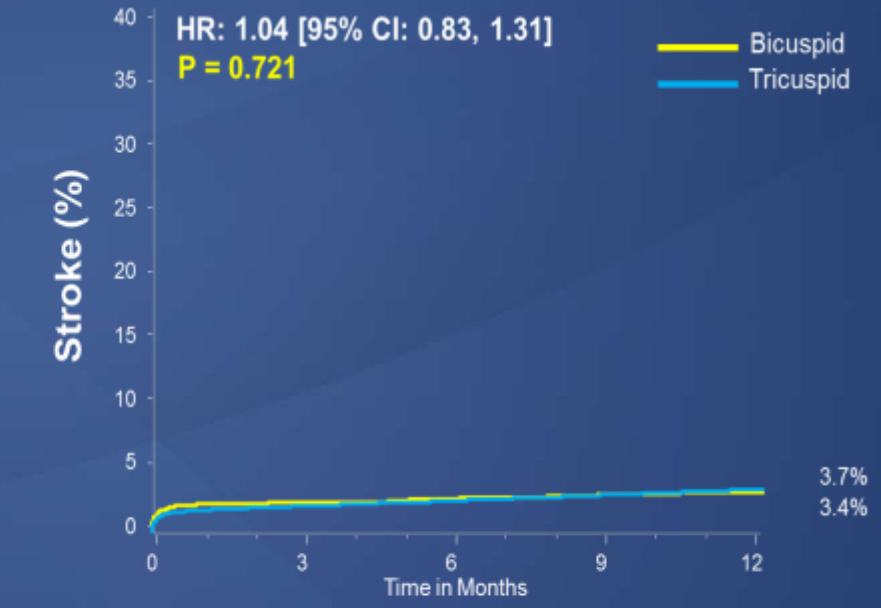
KM estimate %	Bicuspid	Tricuspid AS	p-value
All-cause mortality	2.6	2.5	0.82
All stroke	**2.4**	**1.6**	**0.02**
Life-threatening bleeding	0.1	0.1	0.99
Major vascular complication	0.9	1.0	0.68
New pacemaker	**9.1**	**7.5**	**0.03**
Aortic valve reintervention	0.2	0.3	0.79

1-Year Mortality and All Stroke

Unadjusted Cohort

Bicuspid	2726	1272	1235	1175	947
Tricuspid	79096	41830	40133	37794	30309

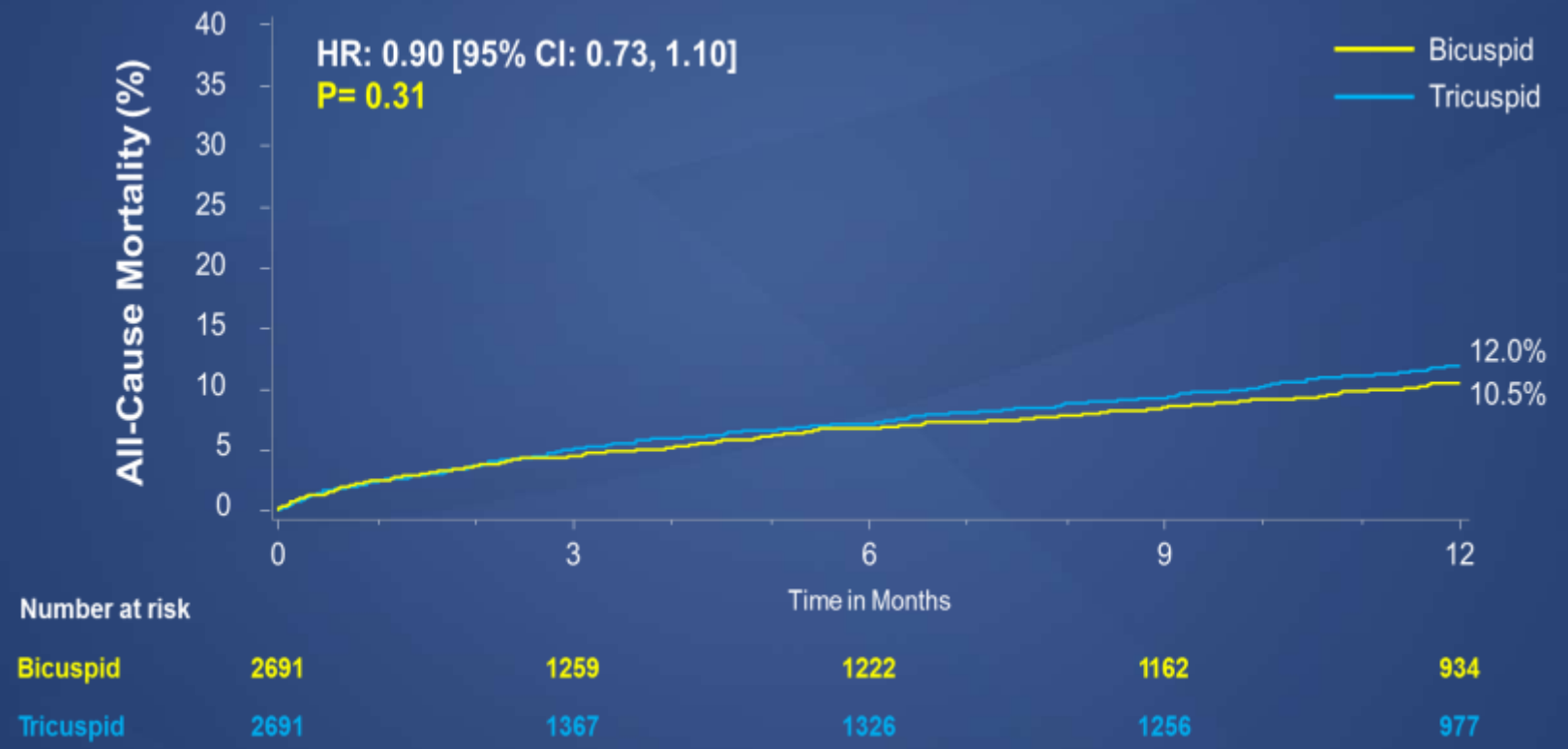
Number at risk



Bicuspid	2726	1247	1209	1148	923
Tricuspid	79096	41050	39266	36851	29459

Number at risk

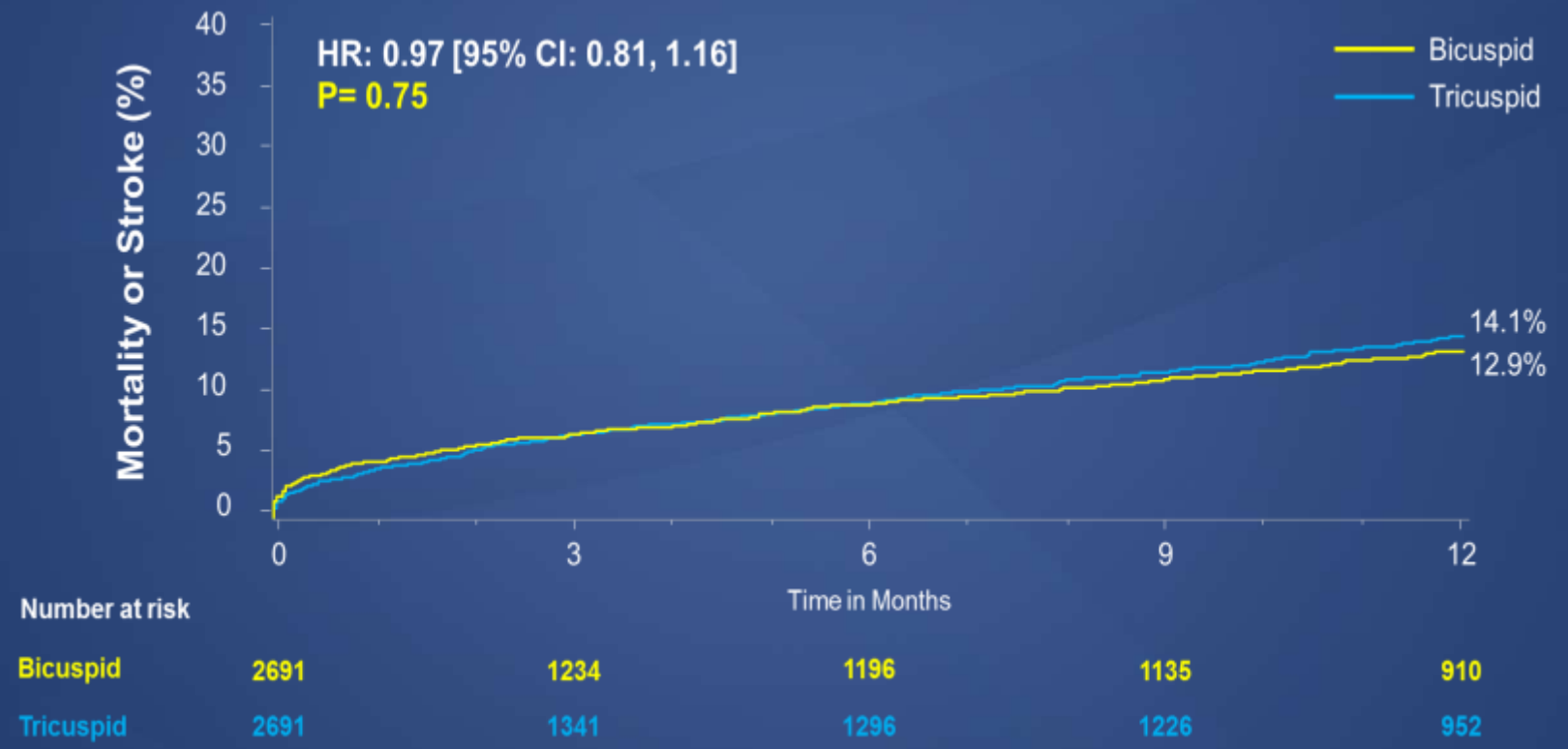
1-Year Mortality:
Matched



Number at risk					
Bicuspid	2691	1259	1222	1162	934
Tricuspid	2691	1367	1326	1256	977

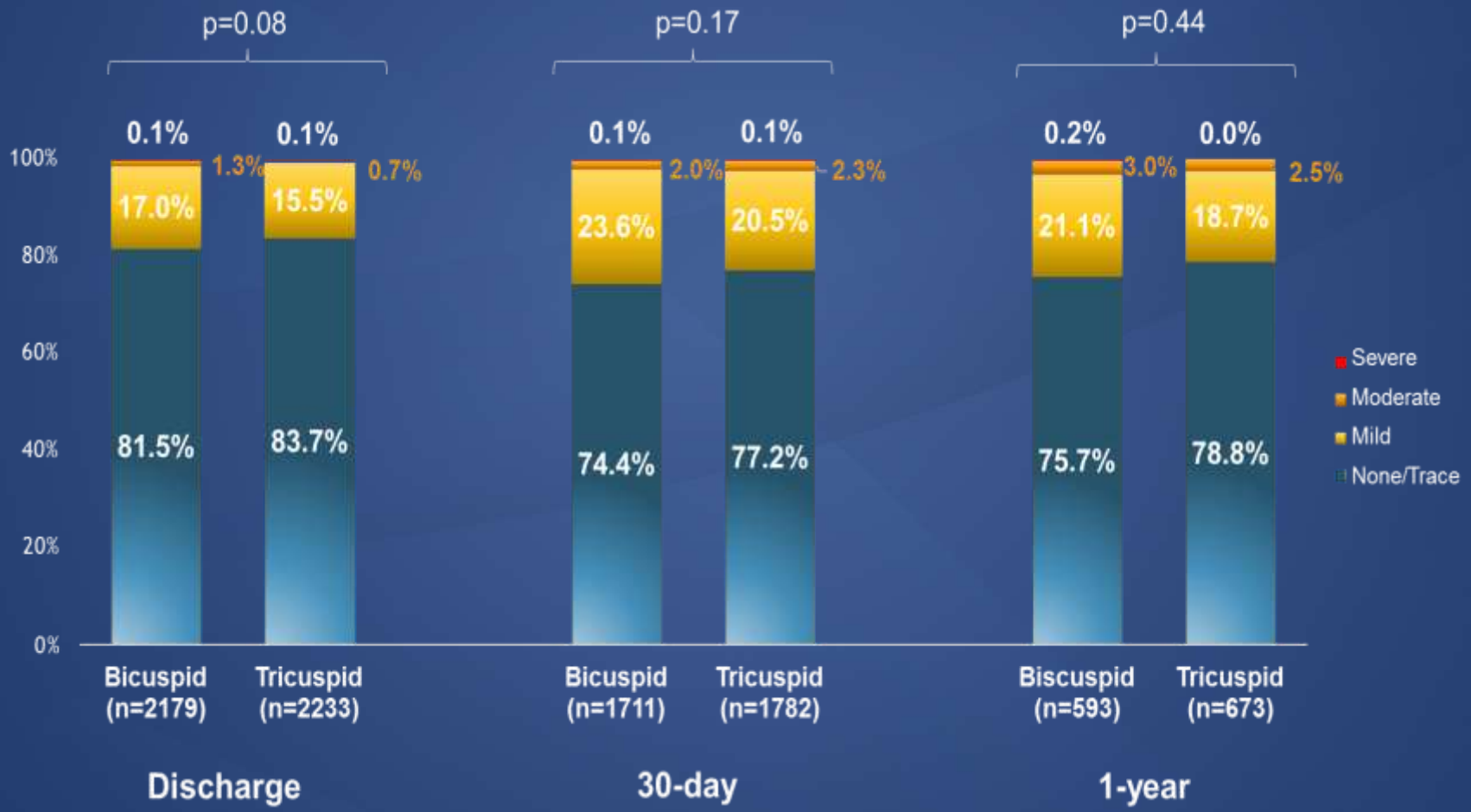
1-Year Stroke:
Matched

1-Year Mortality or Stroke:
Matched

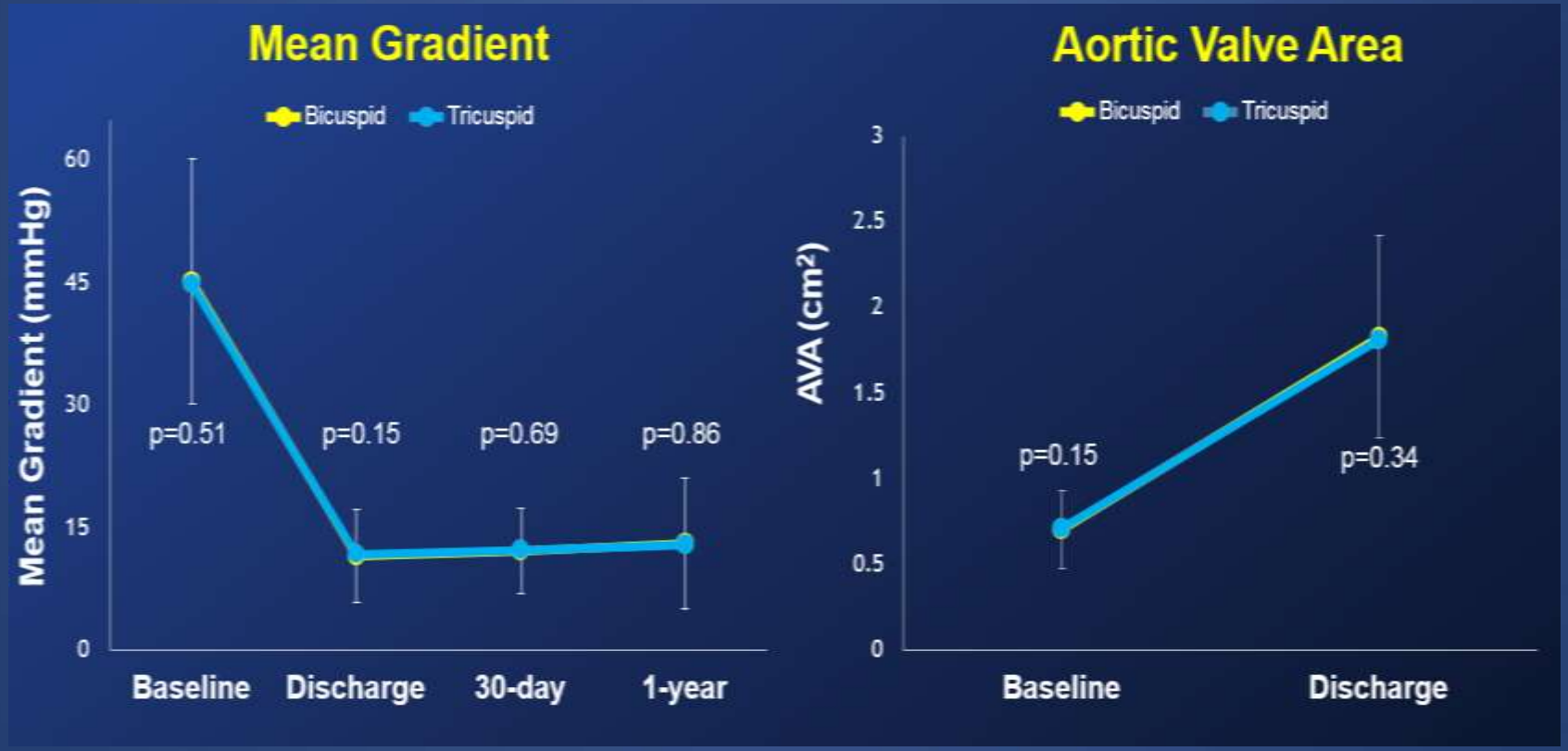


Timing of All-Stroke Events

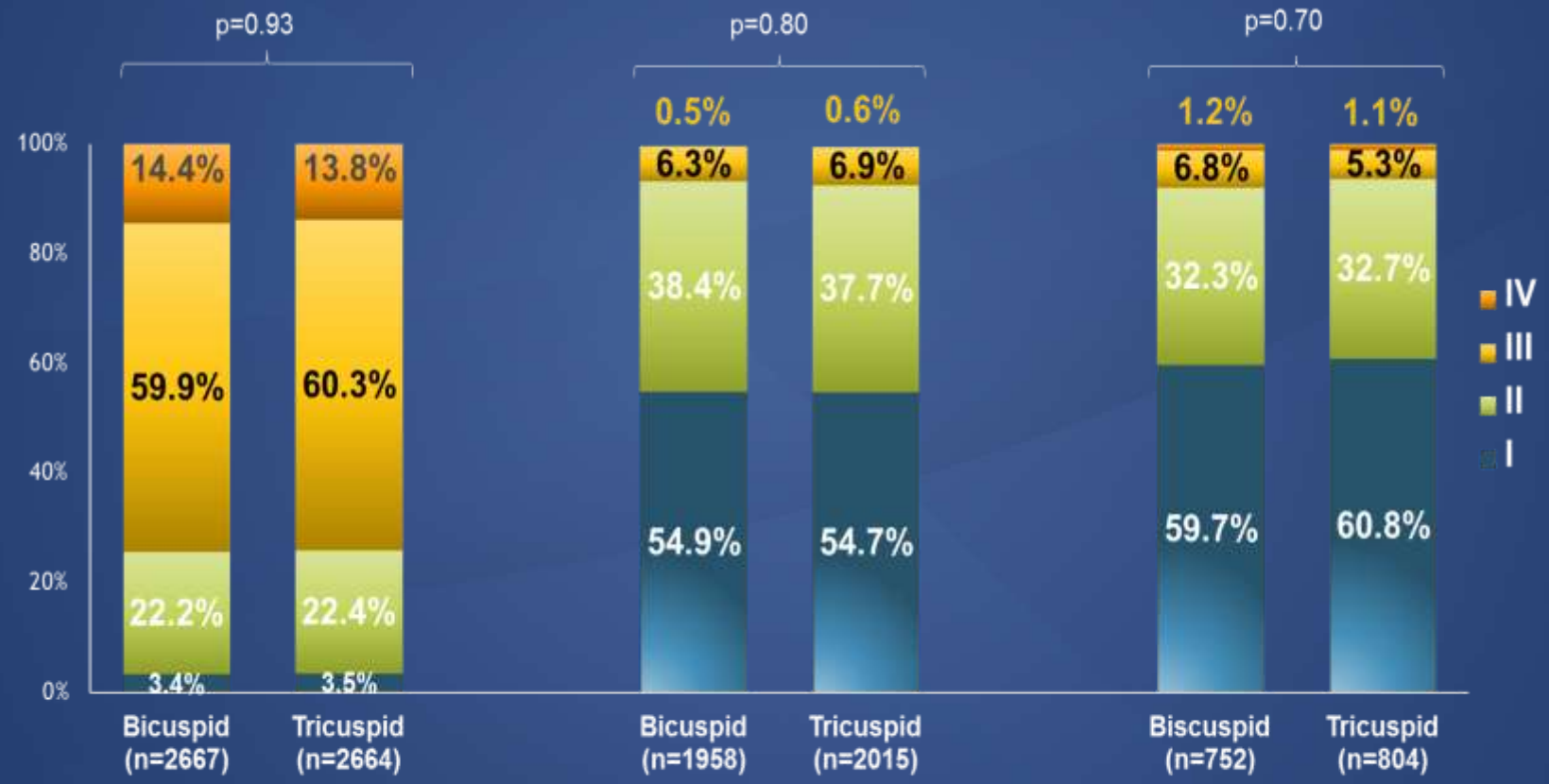
Paravalvular Leak – Matched



Hemodynamics – Matched



NYHA Class – Matched



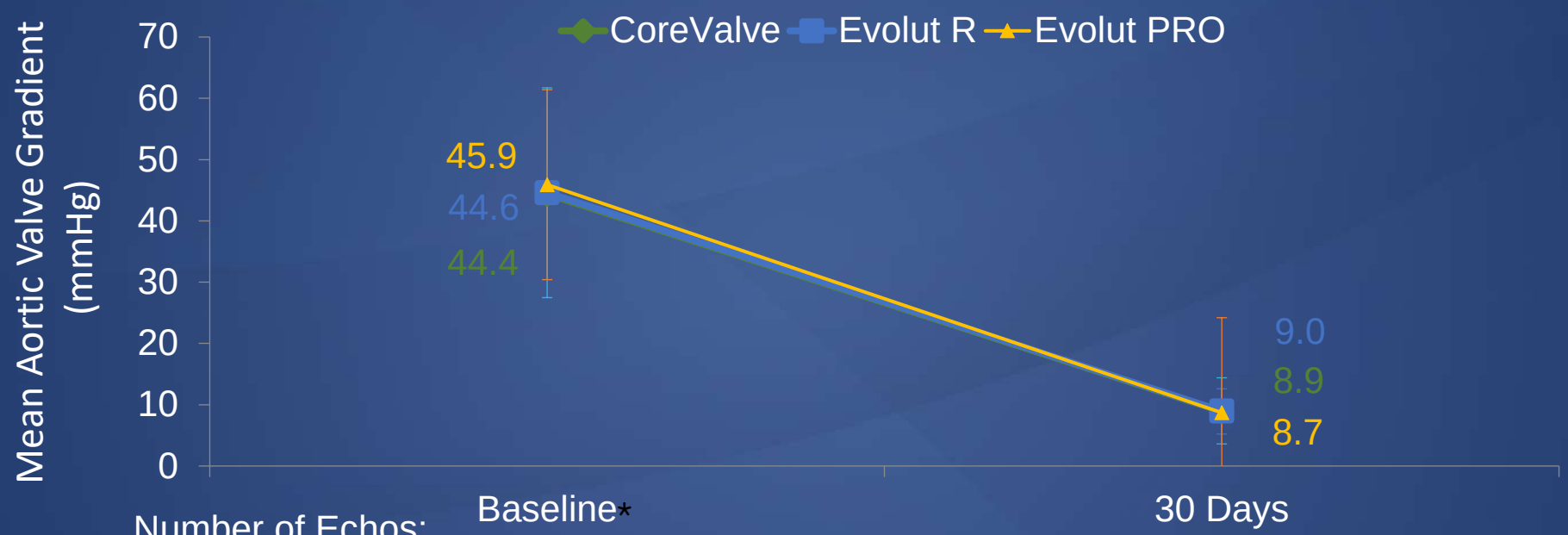
30d outcomes: Self-expanding valve in BAV from STS/ACC TVT registry

Outcome, %	CoreValve (N=319)	Evolut R (N=677)	Evolut PRO (N=236)	*P*-Value	
				CoreValve vs. Evolut R	Evolut R vs. PRO
All-cause mortality	5.4	2.4	3.0	0.01	0.57
Stroke	1.9	3.3	5.6	0.23	0.12
Myocardial infarction	0.3	0.2	0.4	0.58	0.40
Life threatening / major bleeding	7.4	7.1	7.7	0.93	0.77
Major vascular complications	1.9	1.0	1.7	0.27	0.42
Permanent pacemaker	24.7	17.1	11.2	<0.01	0.04
New requirement for dialysis	2.0	1.4	0.0	0.49	0.08
Aortic valve re-intervention	1.7	1.1	0.0	0.46	0.12

John K. Forrest, TVT2019

Hemodynamics: Self-expanding valve in BAV from STS/ACC TVT registry

Mean Aortic Valve Gradient

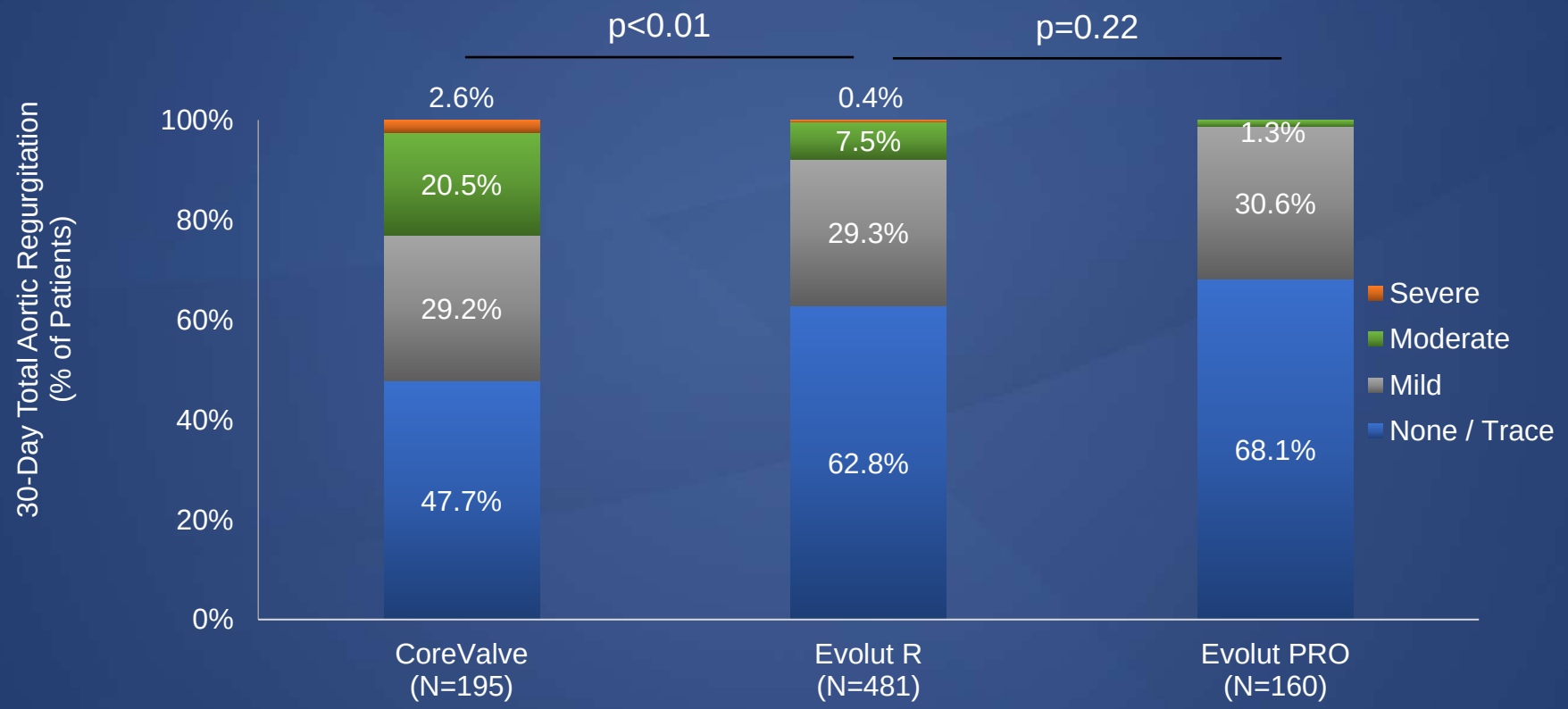


Number of Echos:	Baseline*	30 Days
CoreValve	314	190
Evolut R	663	478
Evolut PRO	236	156

*Baseline subjects are all subjects attempted for the procedure

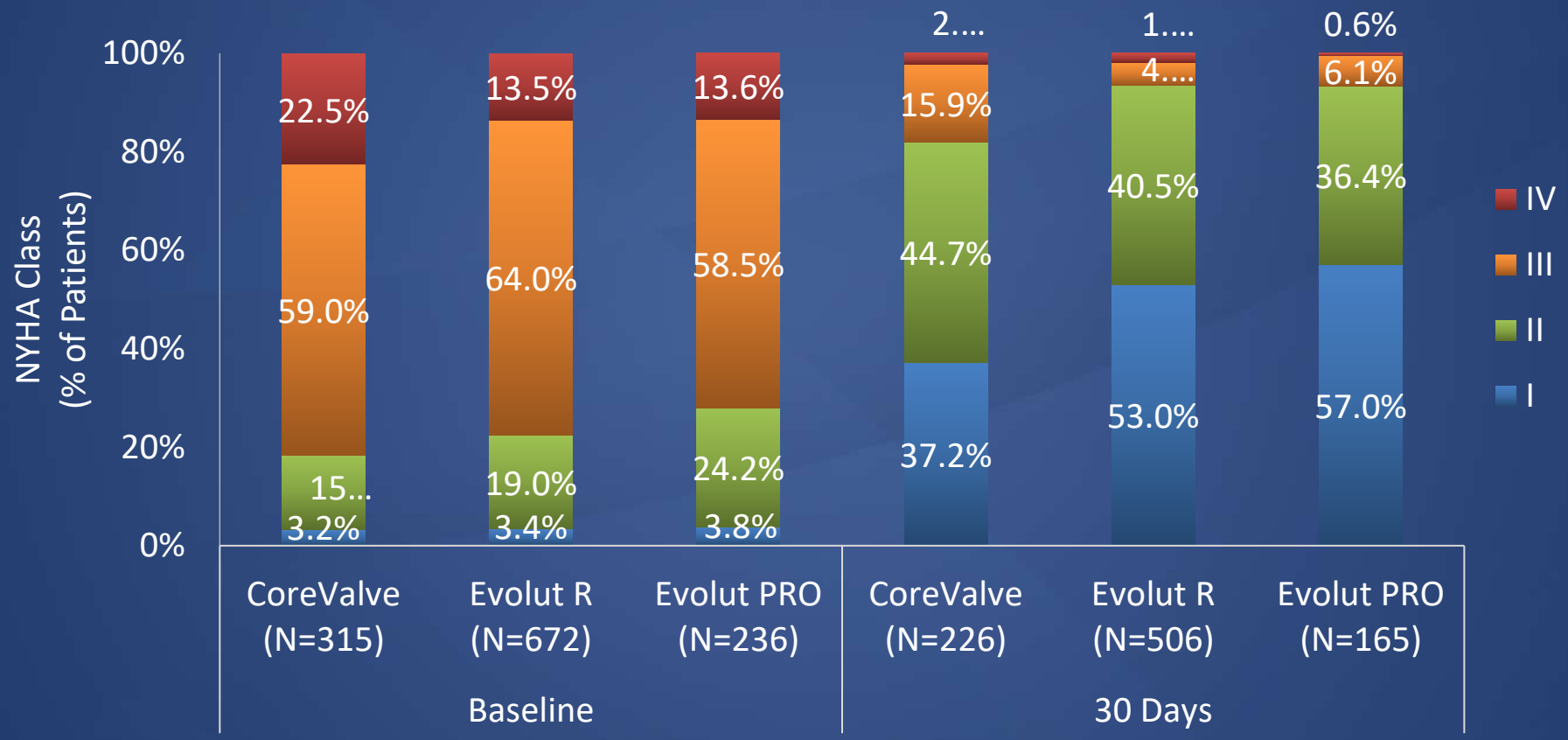
John K. Forrest, TVT2019

30d AR: Self-expanding valve in BAV from STS/ACC TVT registry



John K. Forrest, TVT2019

NYHA class: Self-expanding valve in BAV from STS/ACC TVT registry



John K. Forrest, TVT2019

30d, 1y outcomes: TAVR in Bicuspid vs Tricuspid AS from STS/ACC TVT registry

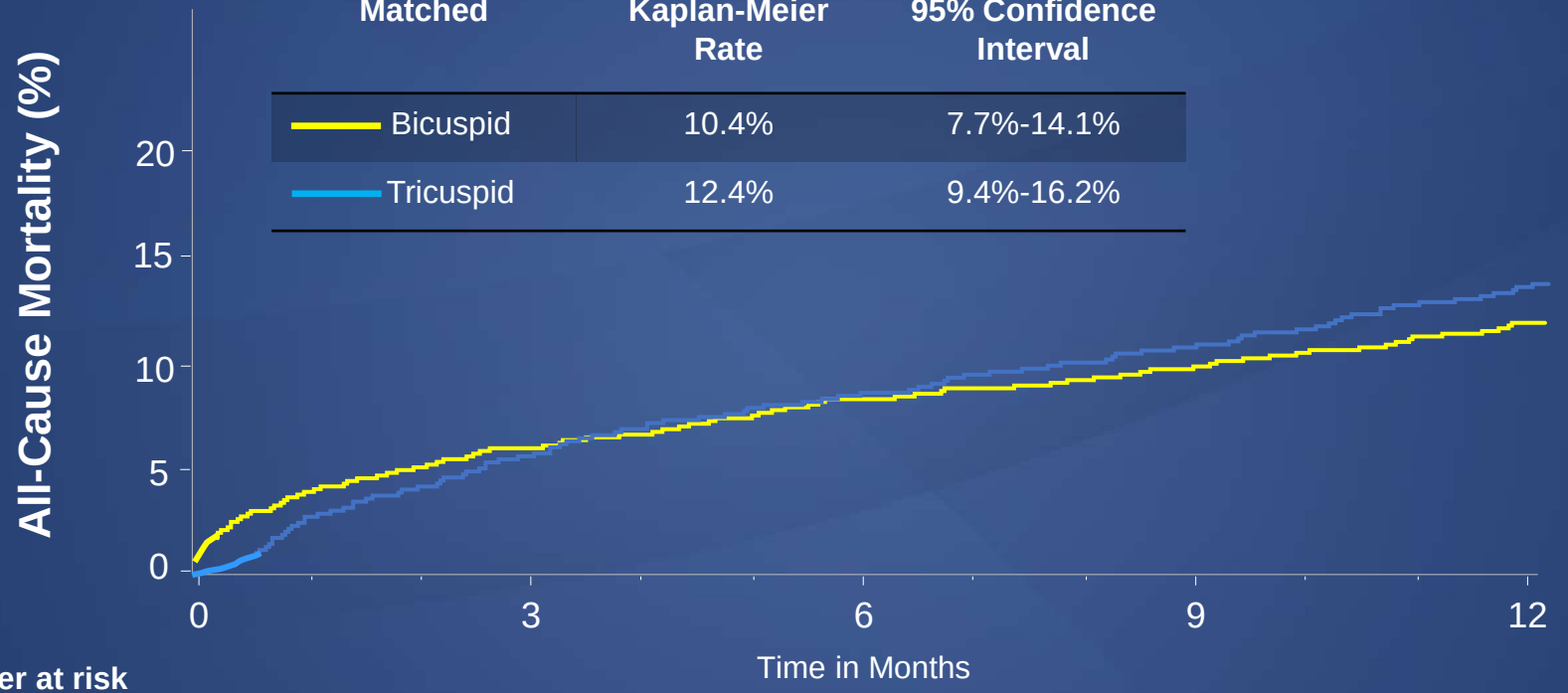
	30 Days			1 Year		
Outcome, n (%)	Bicuspid Group	Tricuspid Group	*p* Value	Bicuspid Group	Tricuspid Group	*p* Value
All-cause mortality	23 (2.6)	15 (1.7)	0.18	62 (10.4)	69 (12.4)	0.63
Stroke	31 (3.4)	25 (2.7)	0.41	33 (3.9)	34 (4.4)	0.93
Myocardial infarction	2 (0.2)	3 (0.3)	0.66	4 (0.7)	5 (0.8)	0.75
Life threatening bleeding	1 (0.1)	1 (0.1)	0.99	2 (0.3)	2 (0.3)	0.98
Valve thrombosis	0 (0.0)	1 (0.1)	0.32	0 (0.0)	1 (0.1)	0.32
Permanent pacemaker	141 (15.4)	126 (13.7)	0.30	145 (16.4)	136 (15.9)	0.52
Percutaneous coronary intervention	2 (0.2)	1 (0.1)	0.56	3 (0.5)	4 (0.8)	0.72
Aortic valve re-intervention	7 (0.8)	1 (0.1)	0.03	11 (1.7)	2 (0.3)	0.01
Valve-related readmission	10 (1.1)	6 (0.7)	0.31	23 (3.8)	18 (3.1)	0.40

John K. Forrest et al, JACC Cardiovasc interv 2020;13: 1749-1759

1-year mortality: TAVR in Bicuspid vs Tricuspid AS

from STS/ACC TVT Registry

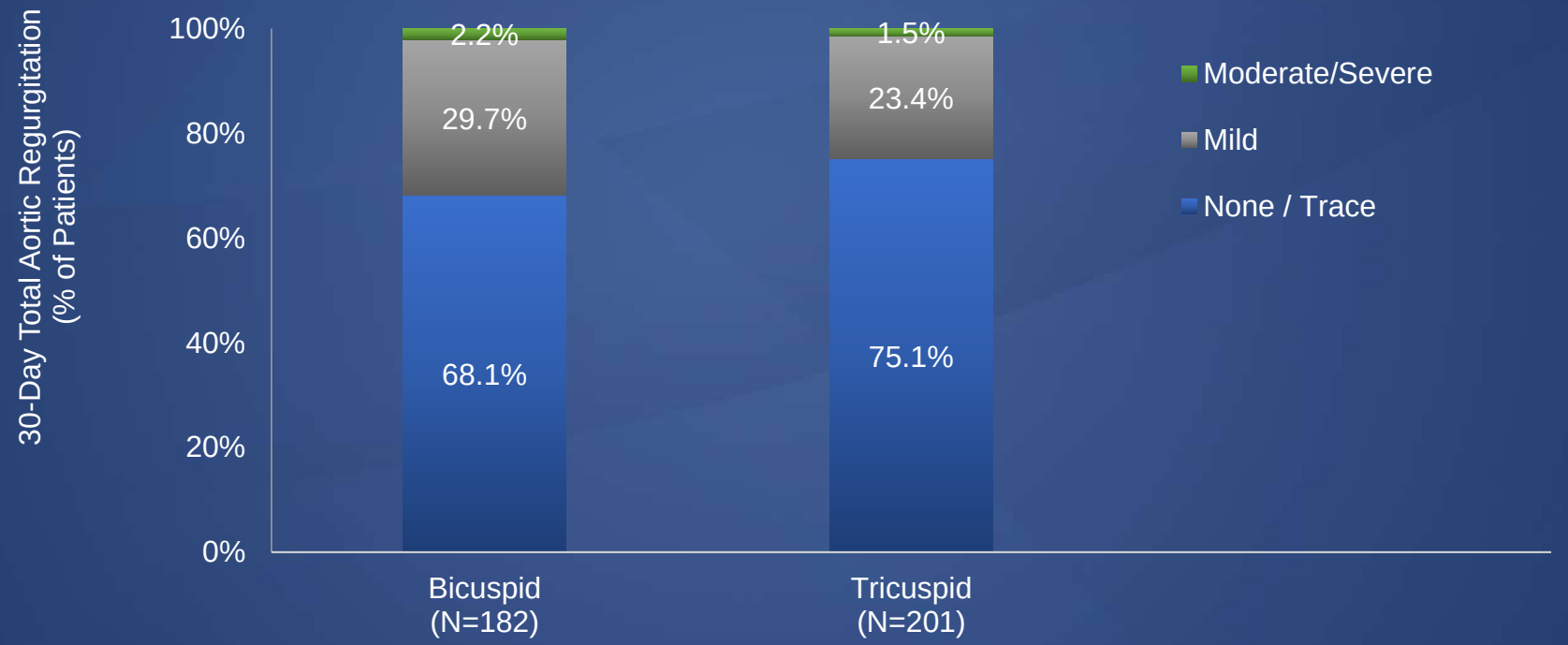
Matched	Kaplan-Meier Rate	95% Confidence Interval
Bicuspid	10.4%	7.7%-14.1%
Tricuspid	12.4%	9.4%-16.2%



Number at risk							
Bicuspid	929	496	456	445	437	425	321
Tricuspid	929	508	474	463	449	432	314

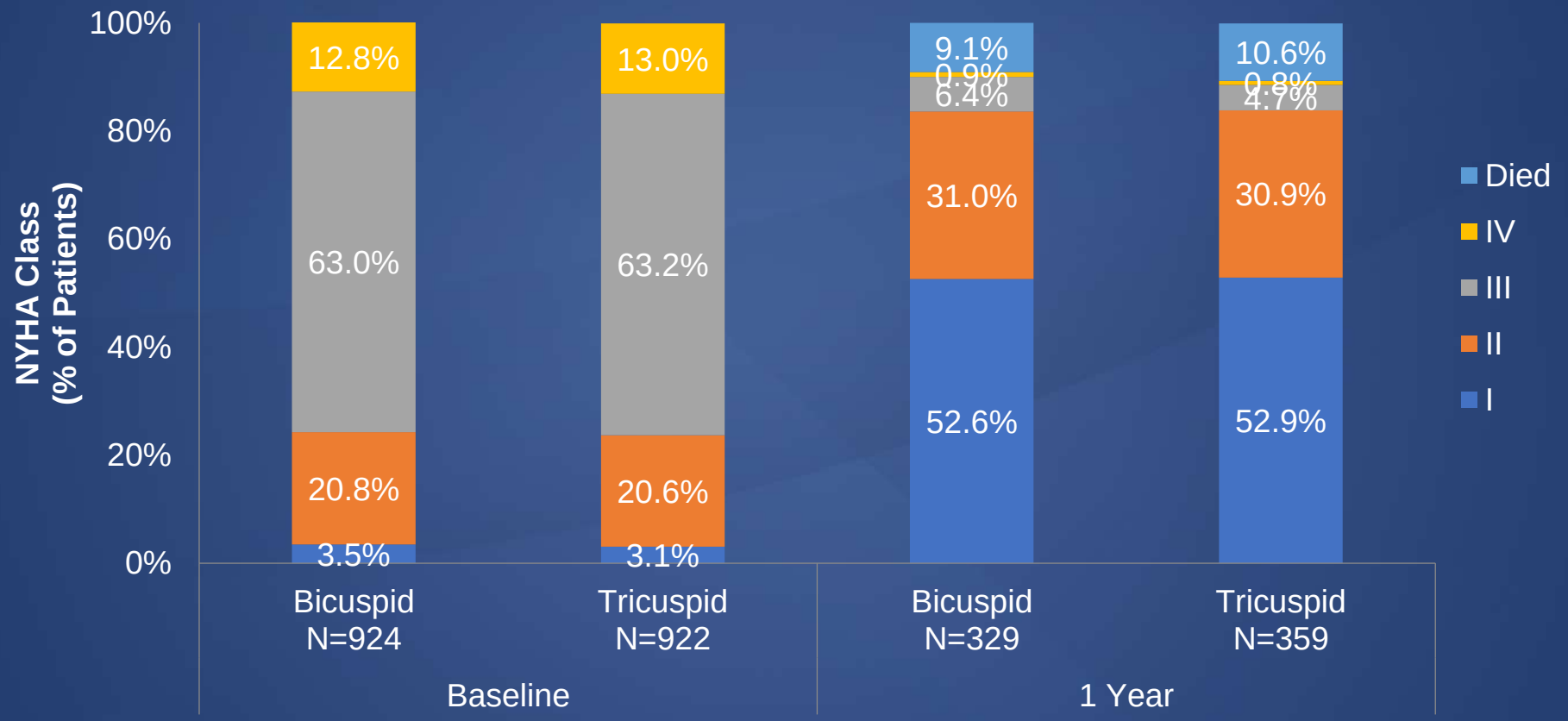
John K. Forrest et al, JACC Cardiovasc interv 2020;13: 1749-1759

30d AR: TAVR in Bicuspid vs Tricuspid AS from STS/ACC TVT registry



John K. Forrest et al, JACC Cardiovasc interv 2020;13: 1749-1759

NYHA class: TAVR in Bicuspid vs Tricuspid AS from STS/ACC TVT registry



John K. Forrest et al, JACC Cardiovasc interv 2020;13: 1749-1759

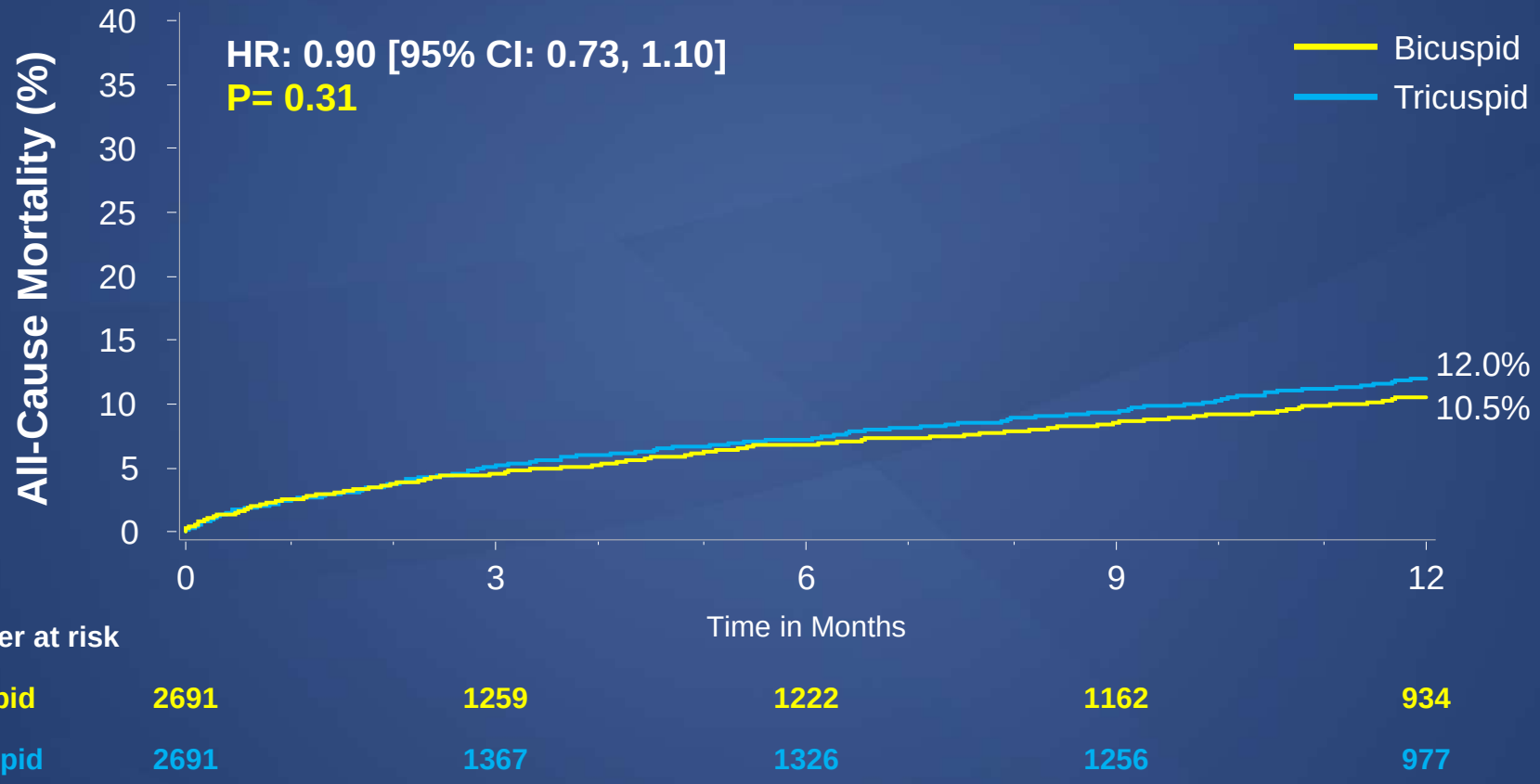
30-day Outcomes: TAVR in Bicuspid
from STS/ACC TVT Registry

KM estimate %	Bicuspid	Tricuspid AS	p-value
All-cause mortality	2.6	2.5	0.82
All stroke	**2.4**	**1.6**	**0.02**
Life-threatening bleeding	0.1	0.1	0.99
Major vascular complication	0.9	1.0	0.68
New pacemaker	**9.1**	**7.5**	**0.03**
Aortic valve reintervention	0.2	0.3	0.79

Raj R. Makkar et al: JAMA 2019;321:2193-202

1-year mortality: TAVR in Bicuspid vs Tricuspid AS

from STS/ACC TVT Registry (PS matching)

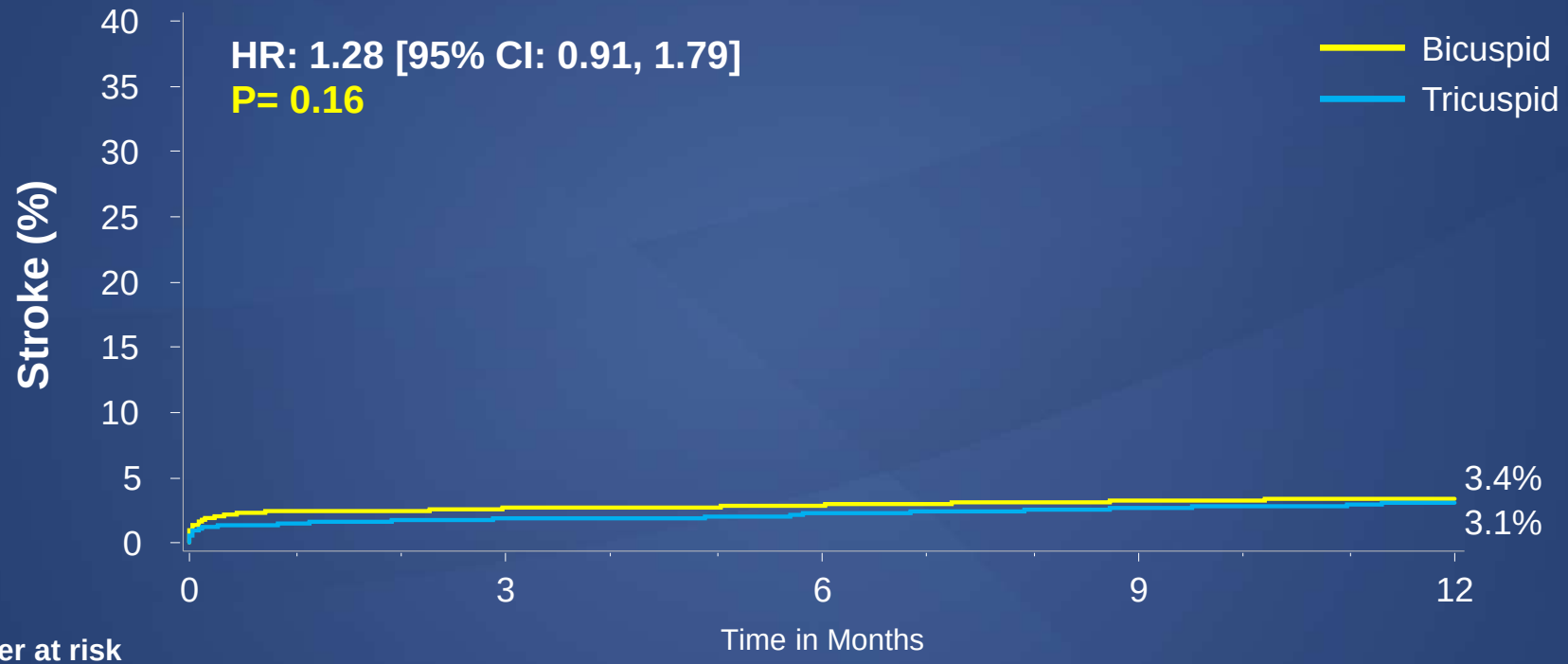


Number at risk					
Bicuspid	2691	1259	1222	1162	934
Tricuspid	2691	1367	1326	1256	977

Raj R. Makkar et al: JAMA 2019;321:2193-202

1-year Stroke: TAVR in Bicuspid vs Tricuspid AS

from STS/ACC TVT Registry (PS matching)

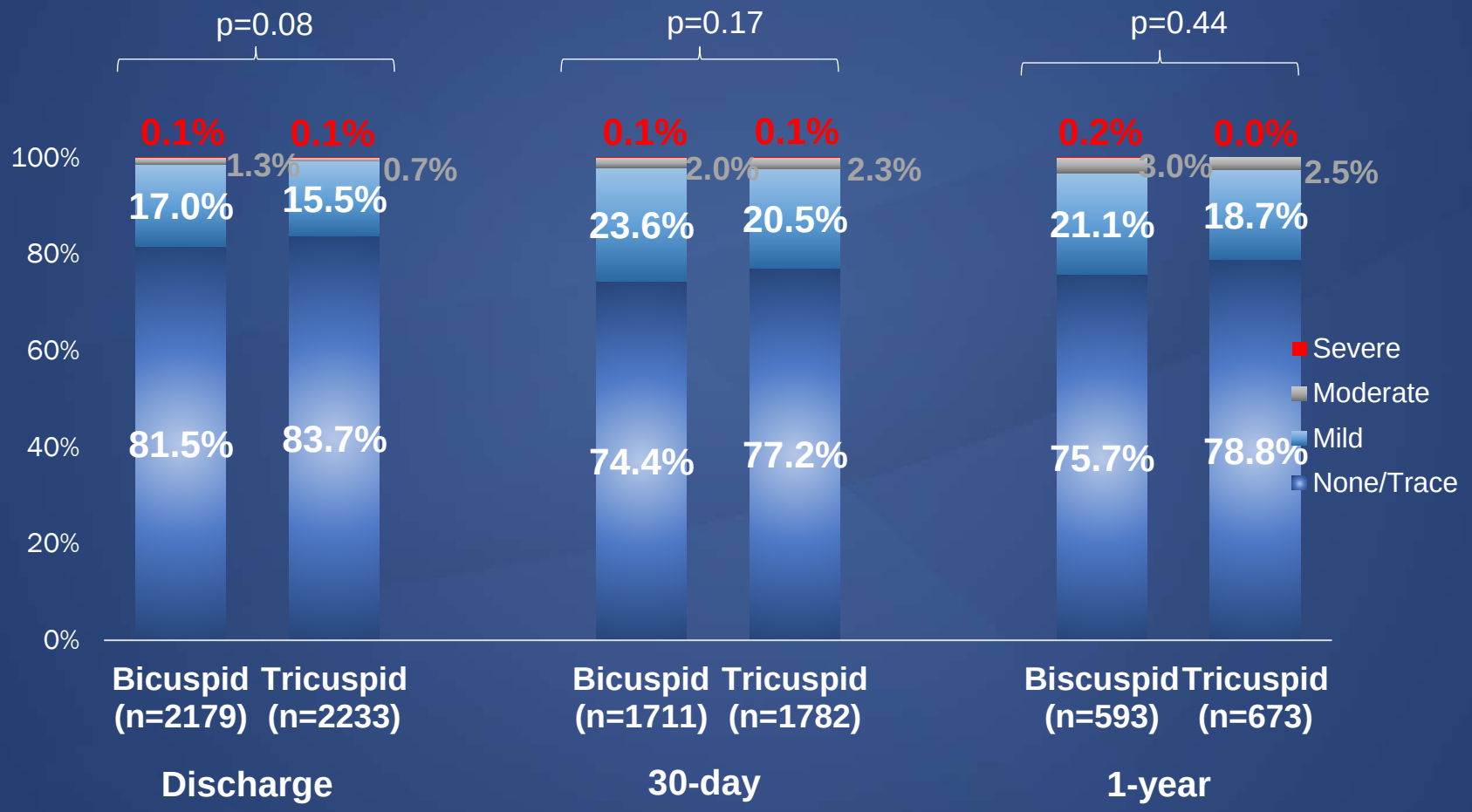


Number at risk					
Bicuspid	2691	1234	1196	1135	910
Tricuspid	2691	1341	1296	1226	952

Raj R. Makkar et al: JAMA 2019;321:2193-202

Paravalvular leakage: TAVR in Bicuspid

from STS/ACC TVT Registry (PS matching)

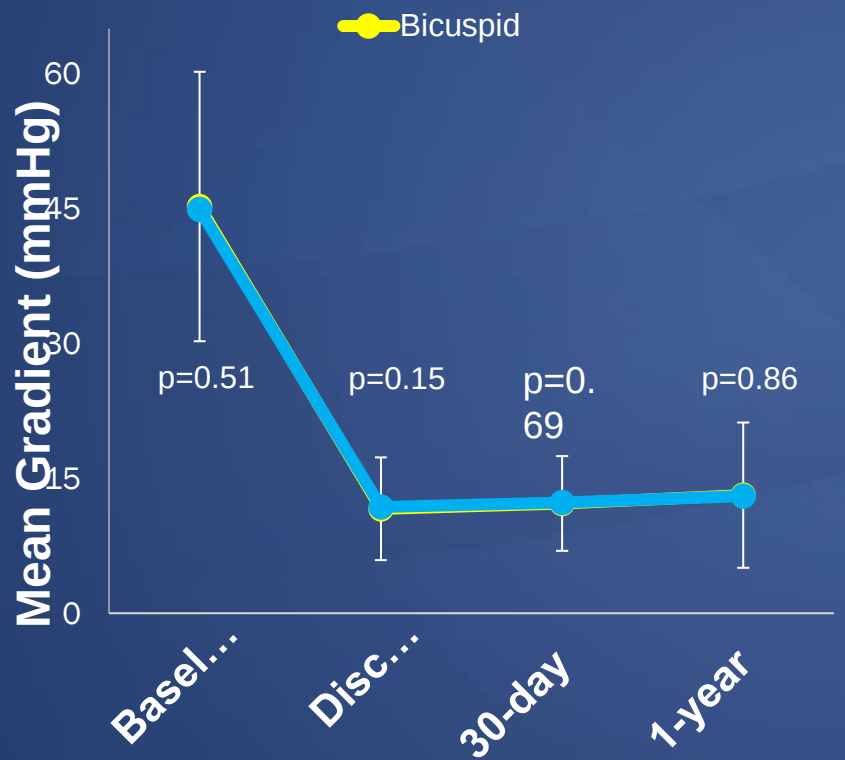


Raj R. Makkar et al: JAMA 2019;321:2193-202

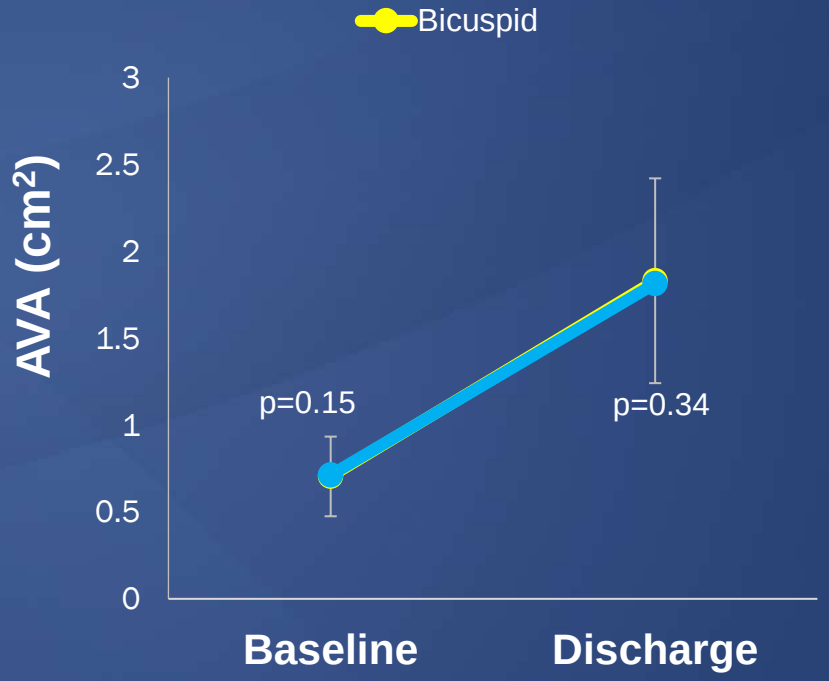
Hemodynamics: TAVR in Bicuspid

from STS/ACC TVT Registry (PS matching)

Mean Gradient



Aortic Valve Area



Raj R. Makkar et al: JAMA 2019;321:2193-202

Outcomes of TAVR in Bicuspid vs Tricuspid AS from STS/ACC TVT Registry

Outcomes	Bicuspid N=5412	Tricuspid N=165547	P Value
Device success, n (%)	5146 (96.0)	158959 (96.7)	0.004
Conversion to open heart surgery, n (%)	39 (0.7)	938 (0.6)	0.139
Need for second valve, n (%)	90 (1.7)	1967 (1.2)	0.002
Post-TAVR mean aortic valve gradient (mmHg)	10.0 (7.0-14.0)	9.0 (7.0-12.0)	<0.001
Post-TAVR mean aortic valve area (cm^2)	1.8 (1.4-2.2)	1.8 (1.5-2.2)	0.473
Post-TAVR moderate/severe aortic insufficiency, n (%)	241 (4.7)	5468 (3.5)	<0.001
Post-TAVR moderate/severe paravalvular aortic insufficiency, n (%)	215 (4.4)	4753 (3.2)	<0.001
Post-TAVR moderate/severe central aortic insufficiency, n (%)	12 (0.3)	429 (0.3)	0.643

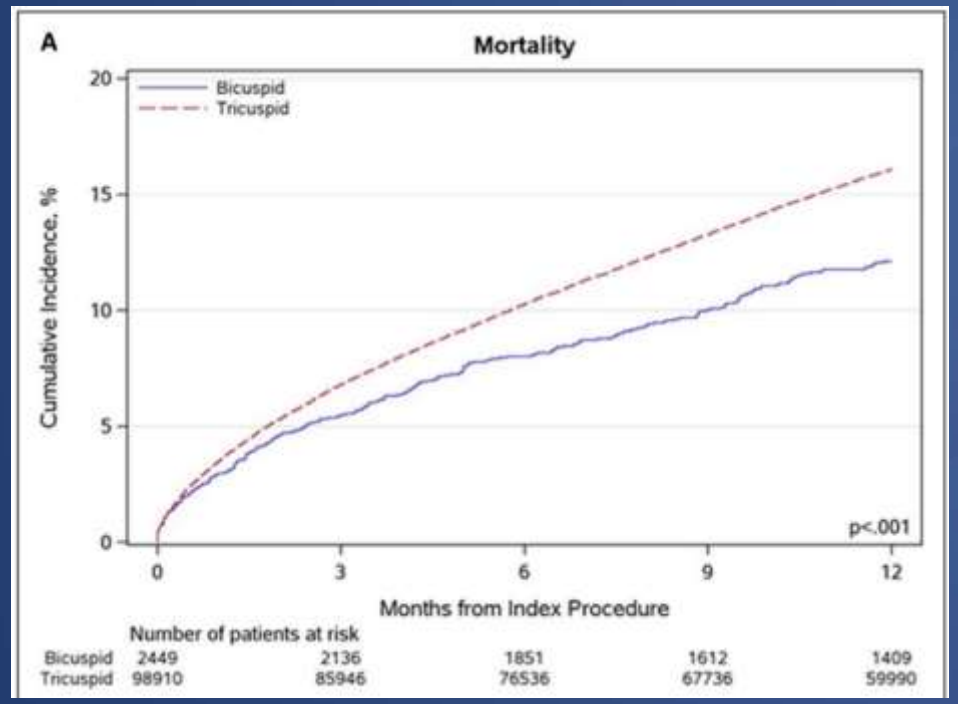
Halim et al:Circulation 2020;141:1071-1079

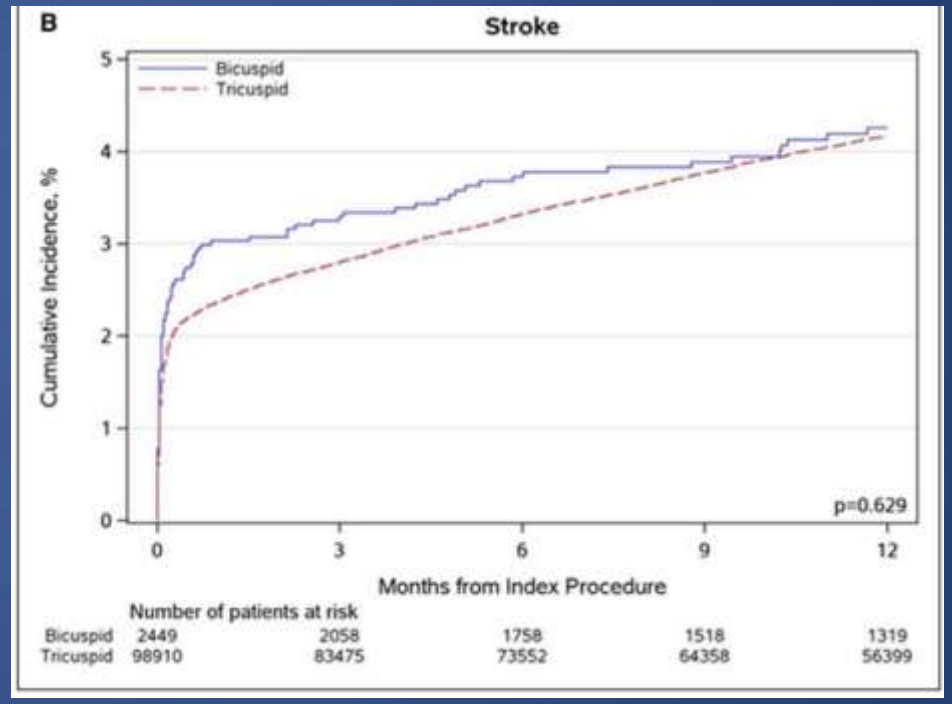
In-hospital Outcomes of TAVR in Bicuspid vs Tricuspid AS from STS/ACC TVT Registry

Outcomes	Bicuspid N=5412	Tricuspid N=165547	P Value
In-hospital death, n (%)	110 (2.0)	3598 (2.2)	0.484
Observed/expected mortality ratio (95% CI)	0.40 (0.33-0.48)	0.31 (0.30-0.32)	0.006
In-hospital stroke, n (%)	117 (2.2)	3131 (1.9)	0.151
In-hospital transient ischemic attack, n (%)	11 (0.2)	318 (0.2)	0.853
In-hospital VARC major or life-threatening bleeding, n (%)	303 (5.7)	10042 (6.2)	0.159
Length of stay (days), n (%)	3.0 (2.0-6.0)	3.0 (2.0-6.0)	<0.001

Halim et al:Circulation 2020;141:1071-1079

1 Year rate of mortality and stroke ; TAVR in Bicuspid vs Tricuspid AS from STS/ACC TVT Registry





Halim et al:Circulation 2020;141:1071-1079

Bicuspid Aortic Valve Morphology and Outcomes After TAVR

Baseline Characteristics

Demographics & Risk Factors	Overall (n = 1115)	Other Comorbidities & Echo parameters	Overall (n = 1115)
Age, years	75.1 ± 9.4	Chronic lung disease	24.9%
Male	58.9%	Atrial Fibrillation	19.8%
NYHA class III or IV	75.3%	Permanent Pacemaker	7.6%
STS score, %	4.2 ± 3.6	Aortic Valve Area (cm^2)	0.7 ± 0.2
Diabetes	25.3%	Mean Gradient (mmHg)	48.5 ± 17.6
Prior PCI	20.7%	LVEF (%)	52.6 ± 15.2
Prior CABG	8.6%	≥ Moderate AR	10.8%
Prior CVA	13.5%	≥ Moderate MR	10.0%

% or mean ± SD

SH Yoon and Raj R. Makkar, Euro PCR 2019

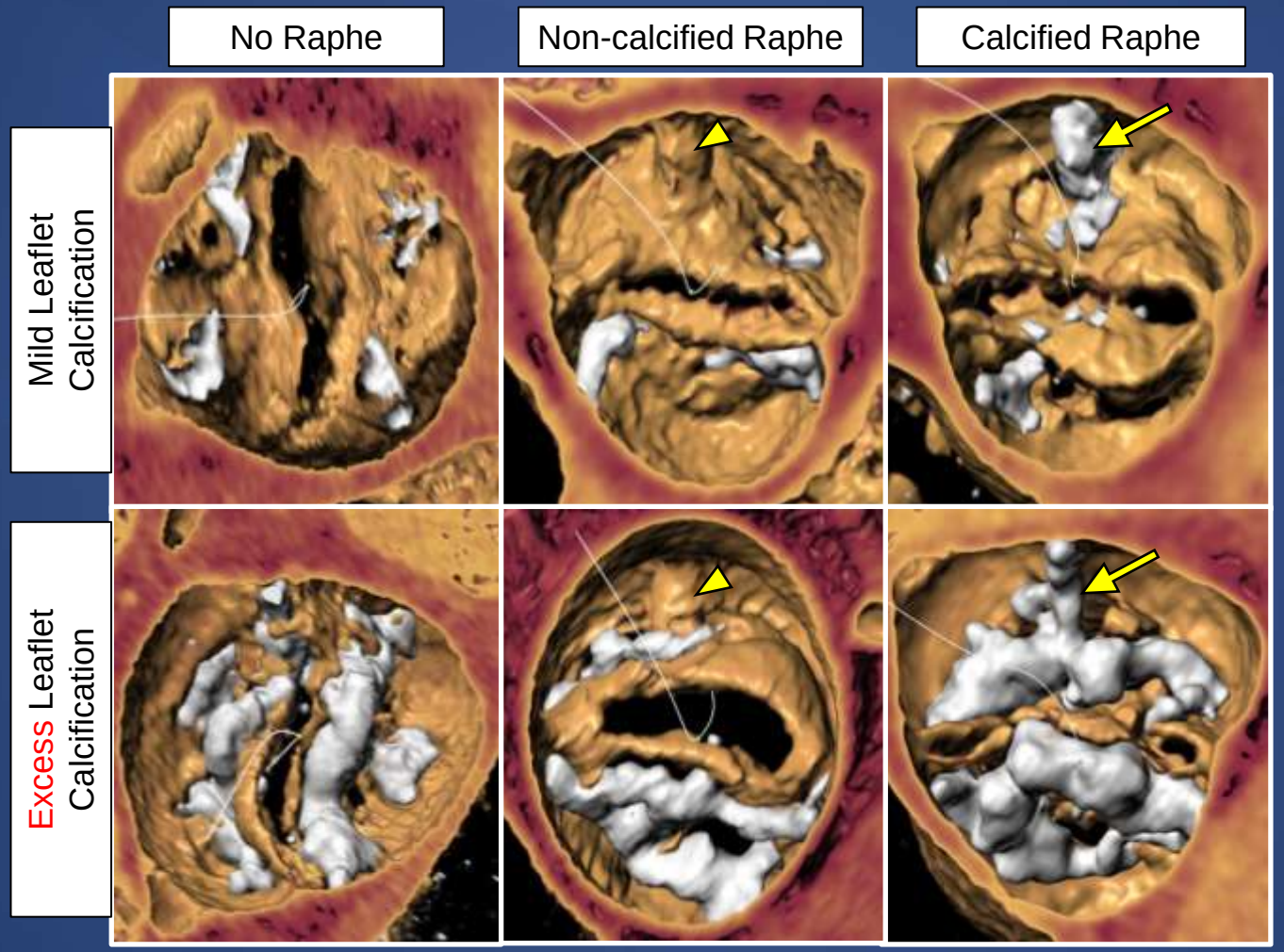
CT Findings and Procedural Data

Characteristic	Overall (n = 1115)
Type of Bicuspid	
No Raphe (type 0)	11.2%
Calcified Raphe (type 1)	46.5%
Non-calcified Raphe (type 1)	42.3%
Calcification Volume in Leaflet (mm^3)	381 (190 – 691)
Aortopathy (diameter ≥ 40 mm)	45.7%
Transfemoral access	90.3%
Device generation	
Early-generation	23.2%
Newer-generation	76.8%

% or median (IQR)

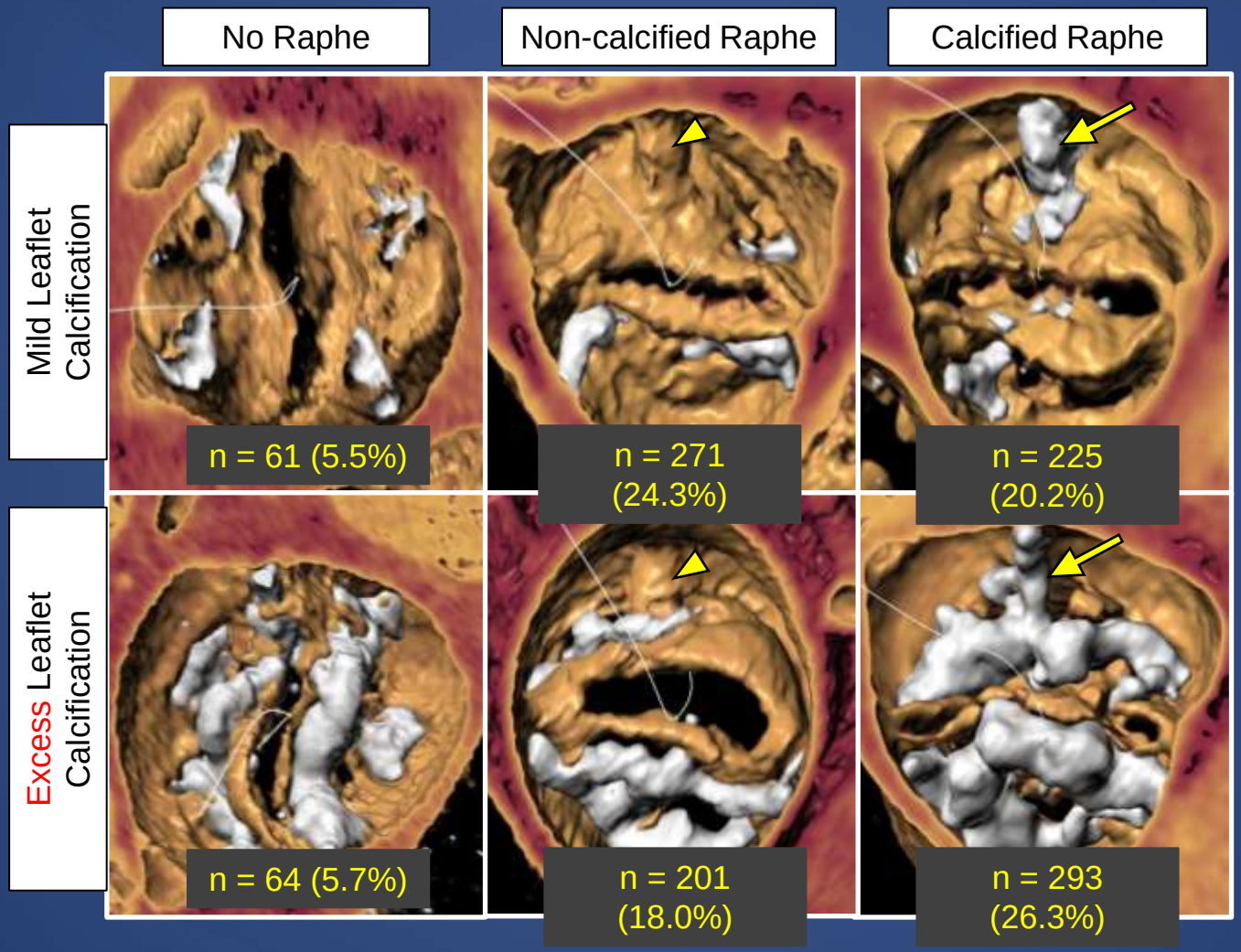
SH Yoon and Raj R. Makkar, Euro PCR 2019

Various BAV Morphology



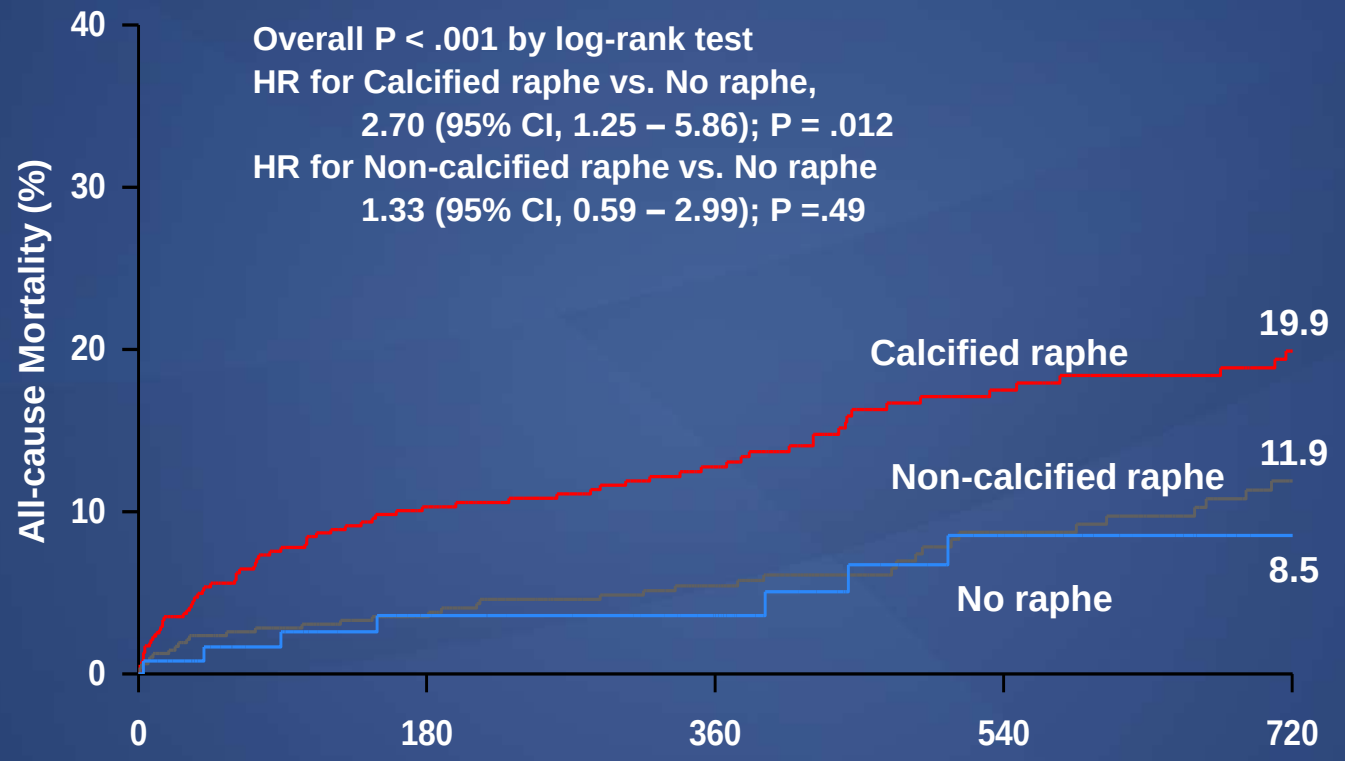
SH Yoon and Raj R. Makkar, Euro PCR 2019

Phenotype Distribution



SH Yoon and Raj R. Makkar, Euro PCR 2019

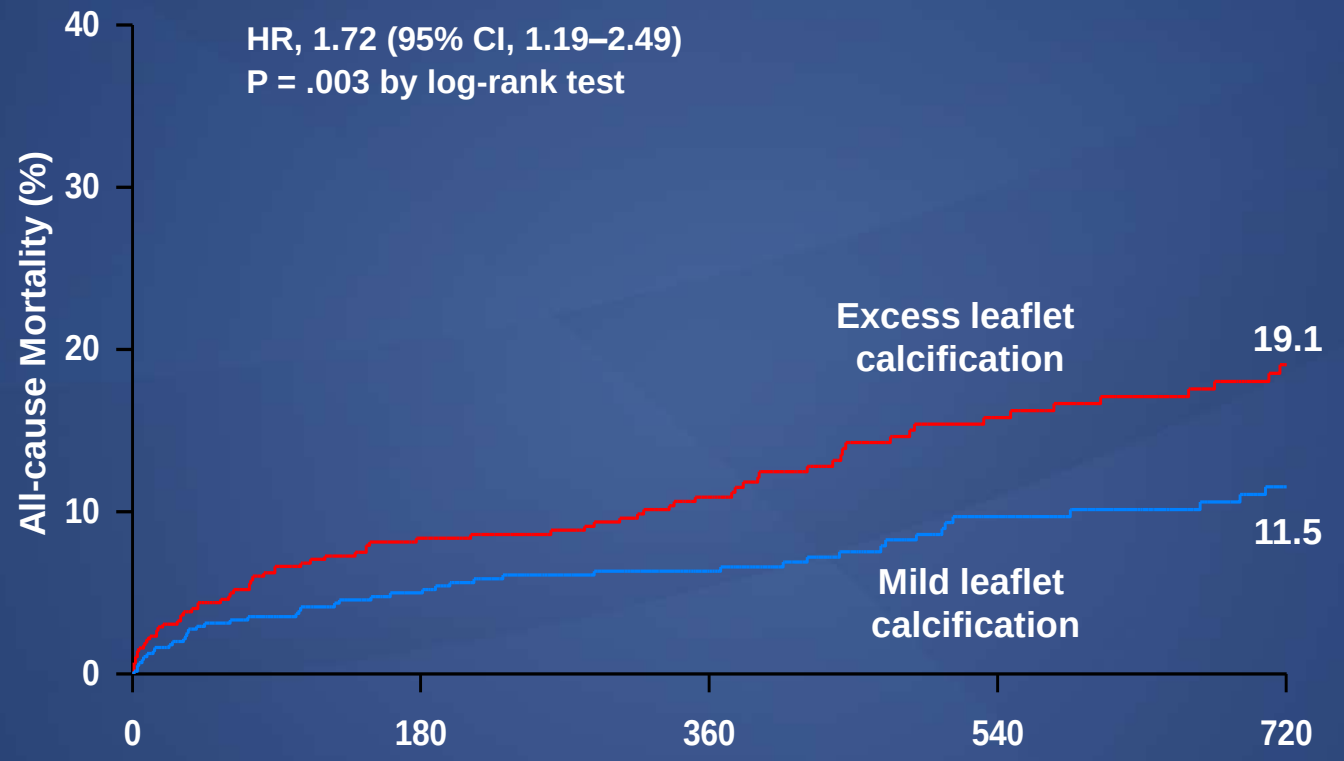
All-cause Death According to Raphe



No. at Risk			
Calcified raphe	518	292	154
Non-calcified raphe	472	310	154
No raphe	125	80	31

SH Yoon and Raj R. Makkar, Euro PCR 2019

All-cause Death According to Leaflet Calcium



No. at Risk			
Excess leaflet ca	558	321	157
Mild leaflet ca	557	361	182

SH Yoon and Raj R. Makkar, Euro PCR 2019

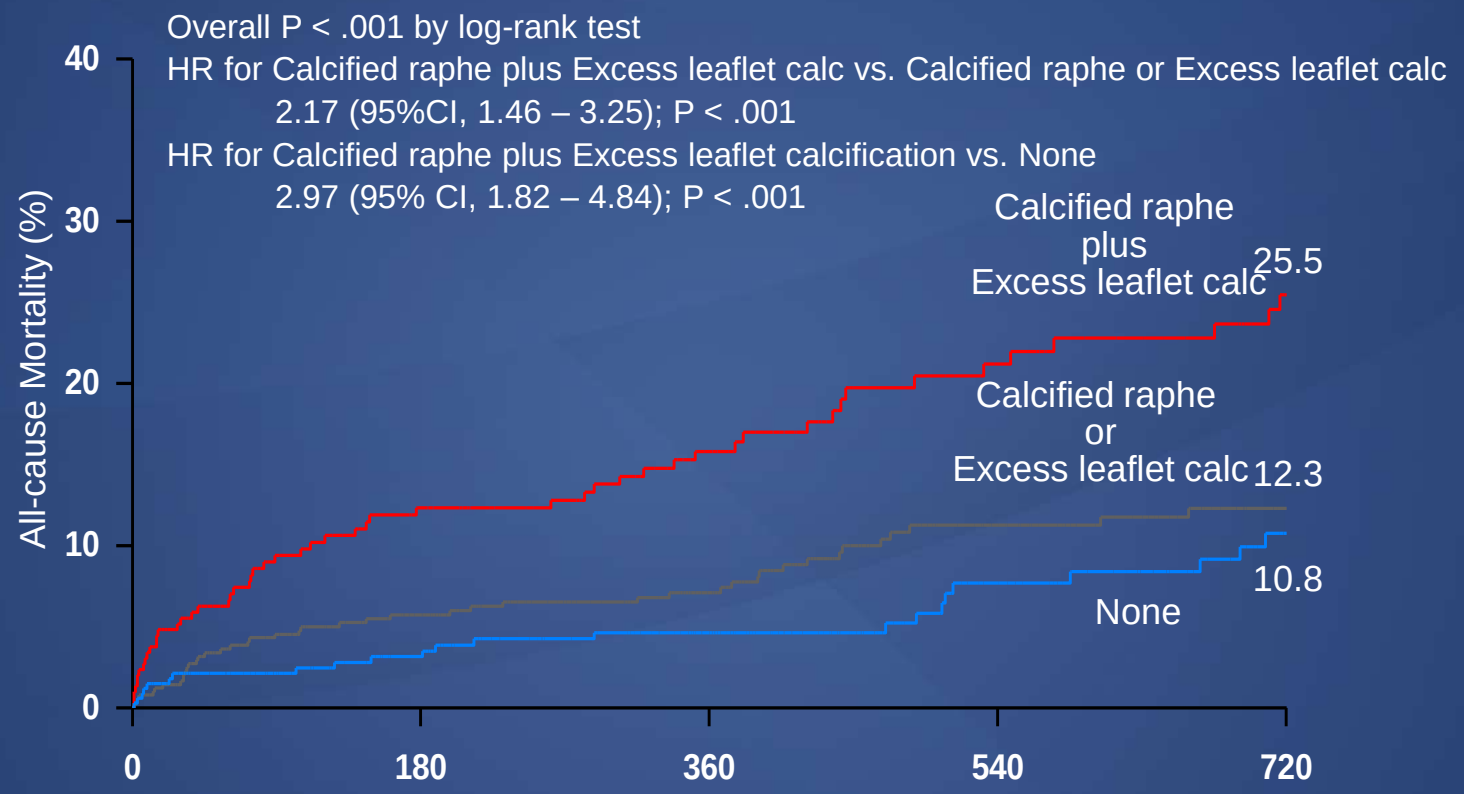
Independent Correlates of All-cause Mortality

	HR (95% CI)	*P* Value
STS score	1.04 (1.01 – 1.08)	0.02
MR ≥ moderate at baseline	1.65 (1.02 – 2.68)	0.04
Type of Bicuspid AV		0.001
No raphe (Sievers' type 0)	Reference	–
Non-calcified raphe (Sievers' type 1)	1.55 (0.69 – 3.50)	0.29
Calcified raphe (Sievers' type 1)	2.80 (1.29 – 6.08)	0.009
Excess leaflet calcification	1.53 (1.05 – 2.22)	0.03
Non-transfemoral access	1.70 (1.05 – 2.75)	0.03
Early-generation devices	1.71 (1.17 – 2.50)	0.005

SH Yoon and Raj R. Makkar, Euro PCR 2019

All-cause Mortality and BAV Phenotype

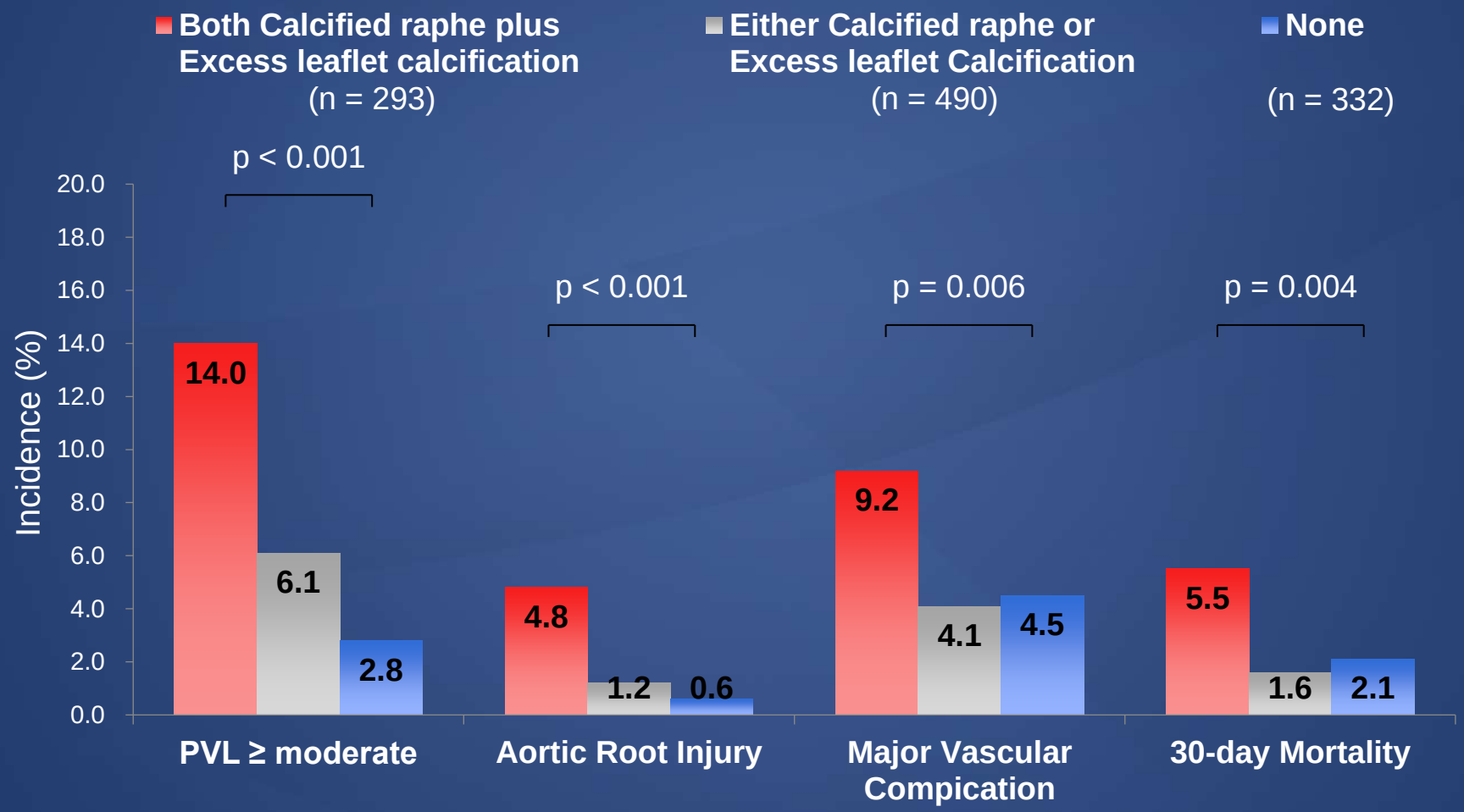
1115 Bicuspid AS patients, 25 Centers



No. at Risk			
Ca-raphe plus excess calc	293	156	80
Ca-raphe or excess calc	490	301	151
None	332	225	108

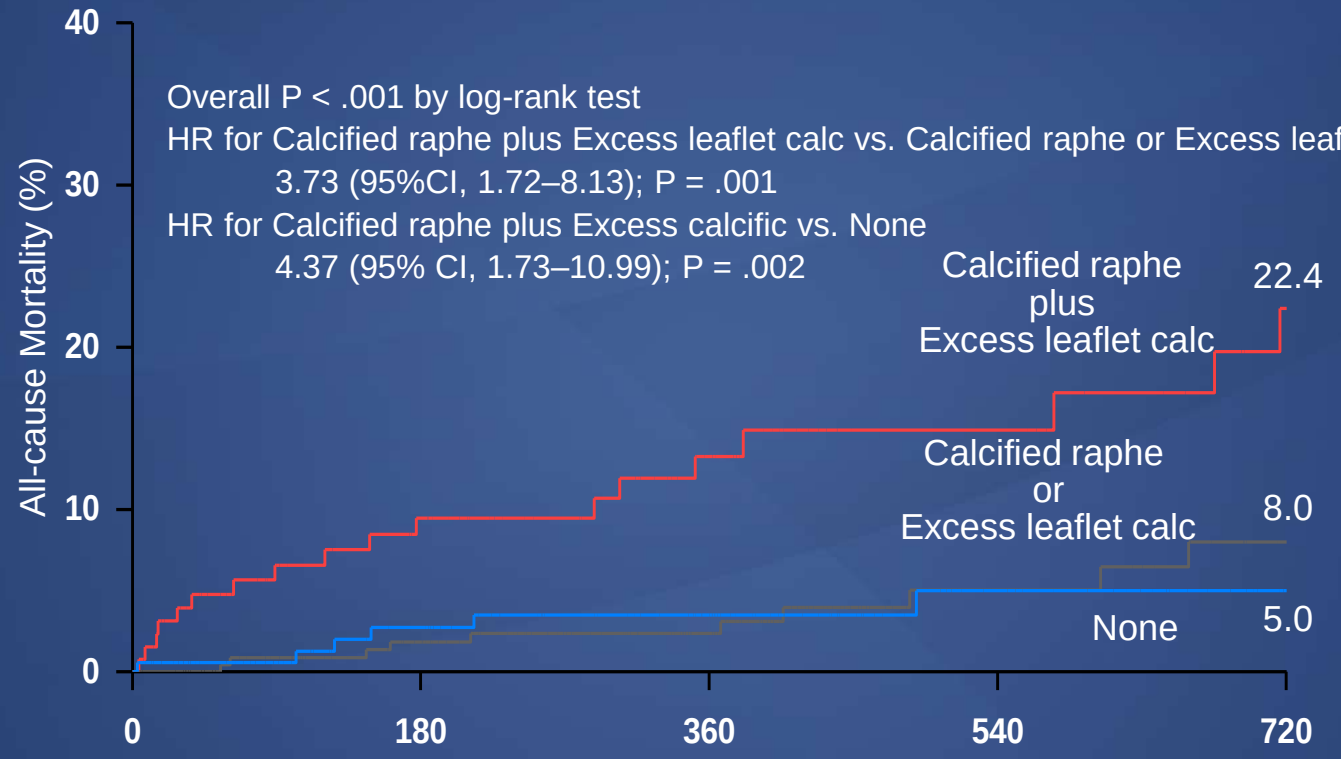
SH Yoon and Raj R. Makkar, Euro PCR 2019

Procedural and 30-day Outcomes According to BAV Phenotype



SH Yoon and Raj R. Makkar, Euro PCR 2019

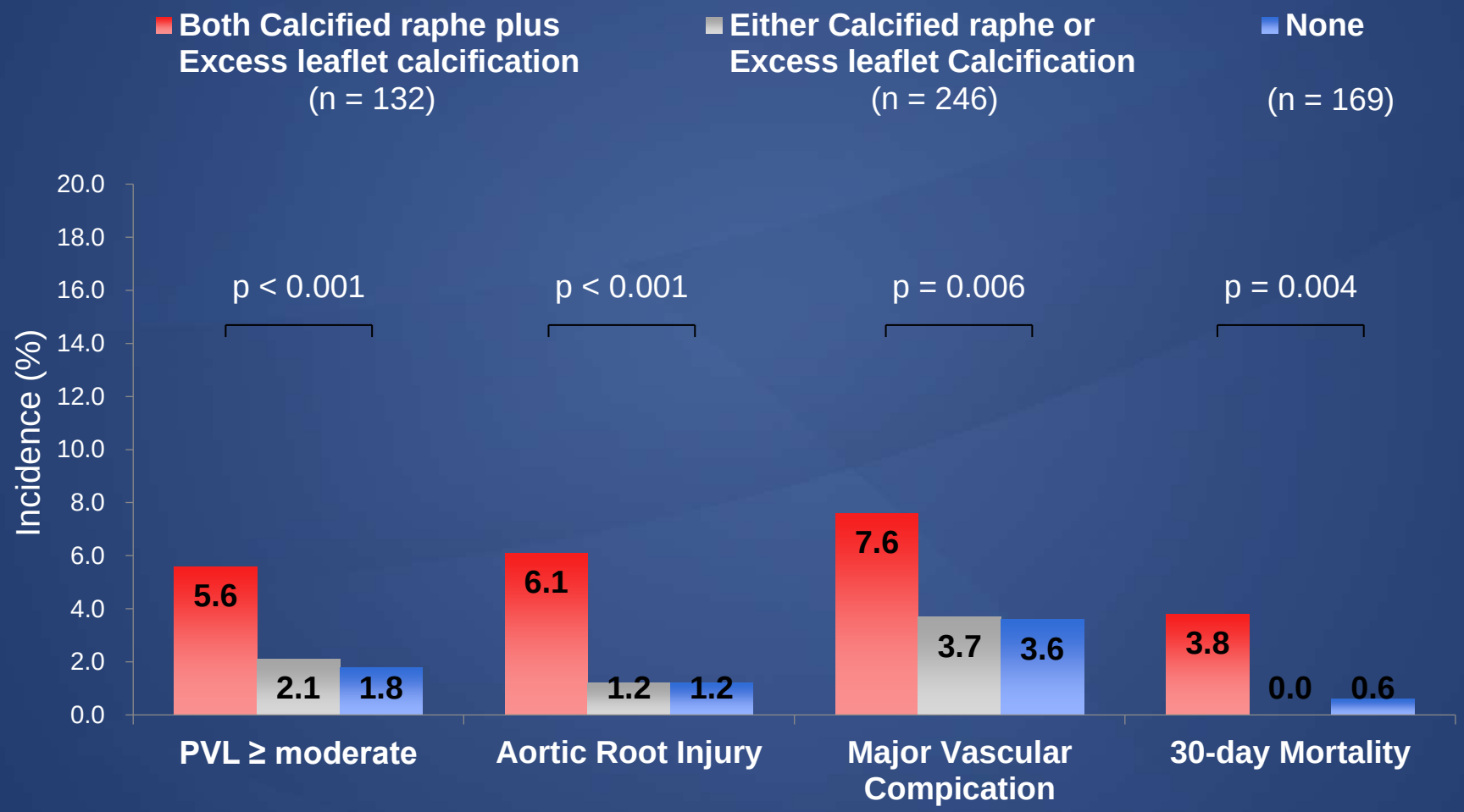
All-cause Mortality and BAV Phenotype
Among Low-Risk Patients with New Devices



No. at Risk			
Ca-raphe plus excess calc	132	61	28
Ca-raphe or excess calc	246	143	54
None	169	102	40

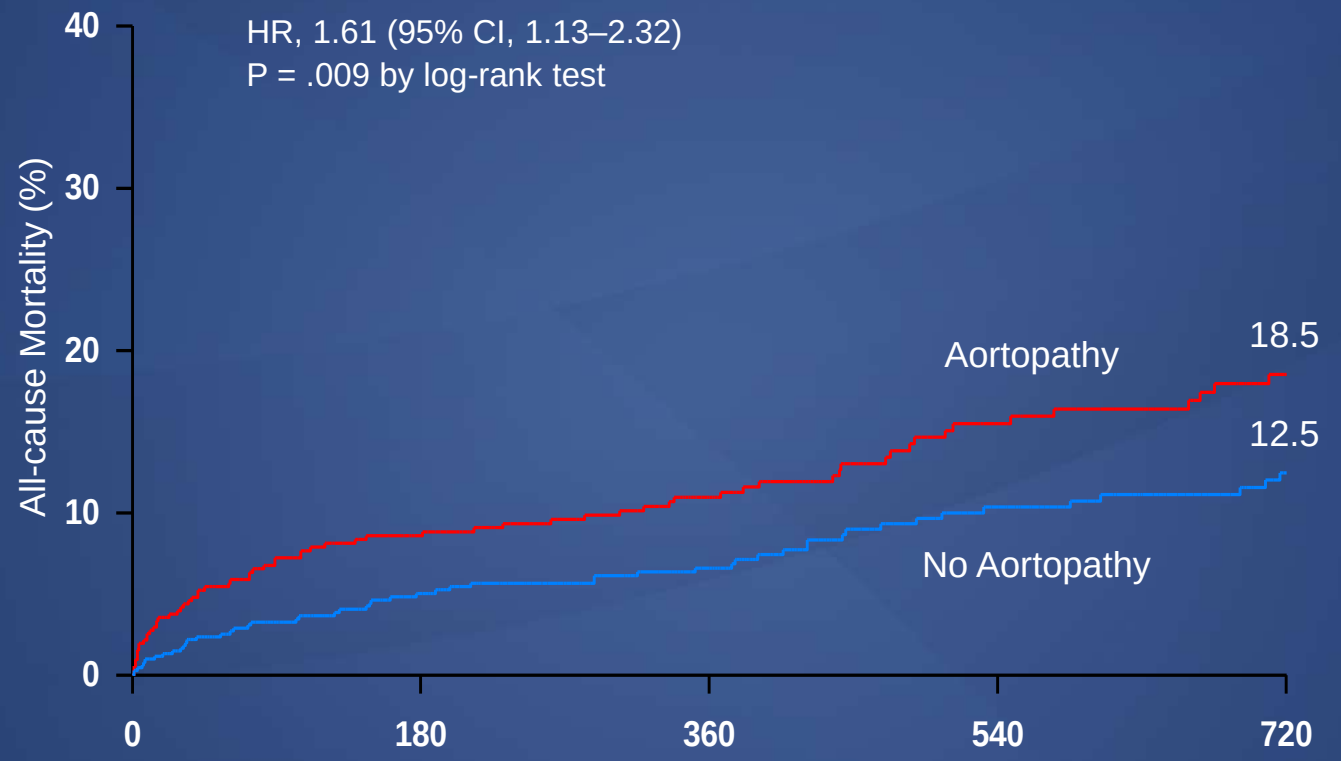
SH Yoon and Raj R. Makkar, Euro PCR 2019

Outcomes According to BAV Phenotype
Among Low-Risk Patients with New Devices



SH Yoon and Raj R. Makkar, Euro PCR 2019

All-cause Mortality and Aortopathy



No. at Risk			
Aortopathy	509	302	147
No Aortopathy	606	380	192

SH Yoon and Raj R. Makkar, Euro PCR 2019

Conclusion

- **BAV morphology** such as ***calcified raphe and excess leaflet calcification*** were independently associated with increased procedural complications and 2-year all-cause mortality

- The impact of BAV morphology on outcomes was consistent in low surgical risk patients as well as in patients who had TAVR with newer generation devices

- Aortopathy was not independently associated with all-cause
mortality

Optimal TAVR for Bicuspid AV

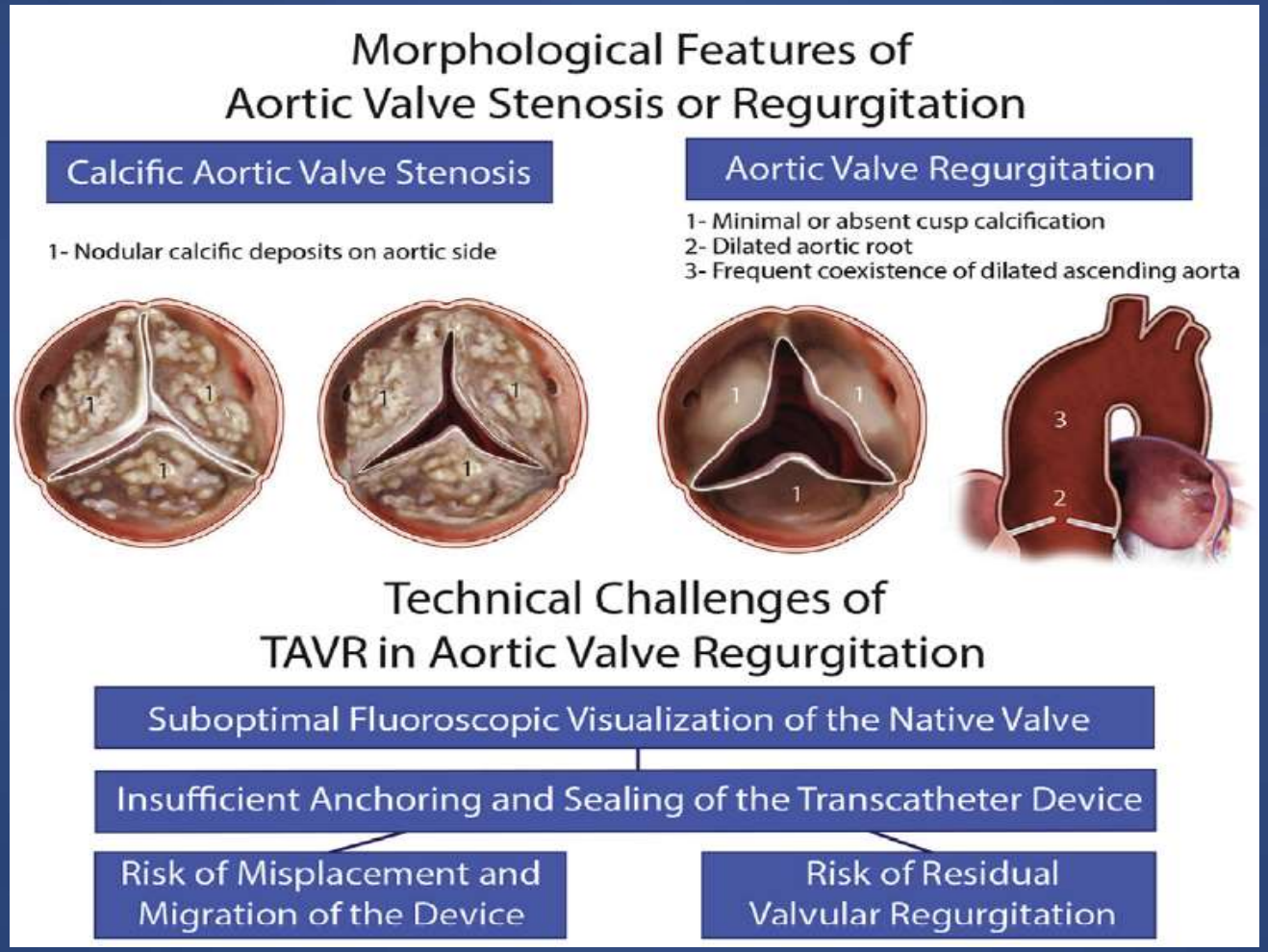
- We need more experiences
- Case selection
- Balloon sizing: Do NOT select too oversize-device in balloon expandable device!
- TAVR for tricuspid and bicuspid AS showed similar long-term mortality. New devices showed better outcomes.
- Relatively high risk of PPM should be considered in younger pts.
- The selected patients with bicuspid AV stenosis would be a candidate of TAVR with better devices.

TAVR for AR

First case

- 1st Generation 25F CoreValve
- 2004 - 2005
- 21 Aug 2004 for Pure AR
- 12 Jul 2004 for ASR

Technical challenges for current TAVI systems



Franzone, et. al. , J Am Coll Cardiol Intv 2016

Early evidence

Self expanding CoreValve

- Better for anchoring in the absence of calcification
- Less risk of annular rupture during deployment
- Better to treat larger anatomies

In early 2 studies

- High early mortality
- Less permanent pacemaker (lack of calcification)
- High rates of PVL and second valve

Jena valve

- Self-expanding Nitinol frame with flexible stent posts
- Porcine root valve
- Clip fixation of native leaflets
- Rapid pacing not required
- Annular range: 21 – 27 mm
  - 3 valve sizes: 23, 25, 27 mm
- 32Fr introducer sheath

Jena valve

Trans-apical, severe AR, 31 patients,
mean age 73.8 ± 9.1, EuroSCORE 23.6 ± 14.5

TABLE 3 VARC-2 Defined Endpoints

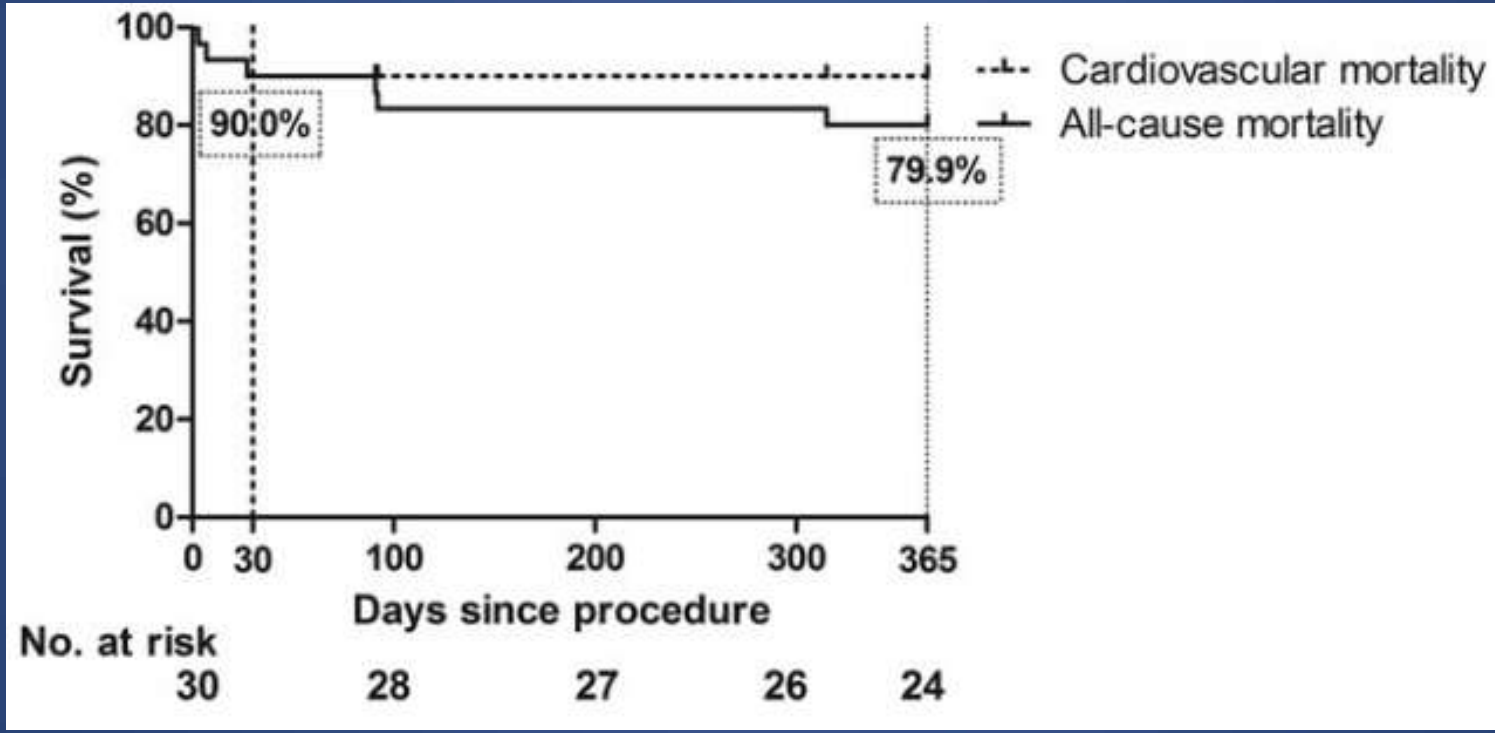
Myocardial infarction	0
Cerebrovascular event	0
Bleeding, major or life-threatening	3 (9.7)
Access site complication	
Minor	1 (3.2)
Major	3 (9.7)
Acute kidney injury	
Stage 1 or 2	6 (19.3)
Stage 3	1 (3.2)
Permanent pacemaker implantation	2 (6.4)*
ICU stay, days	3.2 ± 2.8
In-hospital stay, days	10.8 ± 5.6
Device success	30 (96.8)
Combined early safety endpoint, 30 days	6 (19.3)
All-cause mortality, 30 days	4 (12.9)
Cardiac mortality, 30 days	1 (3.2)
All-cause mortality, 6 months	6 (19.3)
Cardiac mortality, 6 months	1 (3.2)

- **The only TAVI device which is CE marked for treatment of pure AR**
- **Effectively eliminated PVL and the need for a second valve, which led to high device success**

Seiffert, et. al. , J Am Coll Cardiol Intv 2014

Jena valve

Trans-apical, severe AR, 30 patients,
mean age 74.4 ± 9.3, Logistic EuroSCORE I 17.7 ± 14.8



- **All-cause mortality at 1 year – 20% (6/30) with cardiovascular mortality – 10% (3/30)**

Silaschi, et. al. , Catheter Cardiovasc Interv. 2018

Jena valve

Trans-apical, severe AR, 30 patients,
mean age 74.4 ± 9.3, Logistic EuroSCORE I 17.7 ± 14.8

TABLE 3 Composite endpoints according to VARC-I

Composite endpoint	
Device success, no. (%)	24/27 (88.9%)[a]
• Sequential THV, no.	0
• Conversion to open SAVR, no. (%)	1/27 (3.7)
• Function of THV not as intended assessed by echo, no. (%)	2/27 (7.4)[a]
Combined safety endpoint at 30 days, no. (%)	4 (13.3)
• All-cause mortality, no. (%)	3 (10.0)
-Cardiovascular mortality, no. (%)	2 (6.7)
• Major stroke, no. (%)	1 (3.3)
- Valve embolization, no. (%)	1 (3.3)
• Life-threatening or disabling bleeding, no.	0
• Acute kidney injury stage III, no.	0
• Peri-procedural MI, no.	0
-Coronary ostia occlusion, no.	0
• Major vascular complication, no.	1 (3.3)
-Annular rupture, no.	0
• Repeat procedure for valve related dysfunction, no. (%)	1 (3.3)[b]
- Valve migration, no.	0
Combined efficacy at one year, no. (%)	19/26 (73.1)
• All-cause mortality after 30 days, no. (%)	3 (11.1)
-Cardiovascular mortality after 30 days, no. (%)	1 (3.7)
-Life-threatening/disabling bleeding, no. (%)	1 (3.7)
• Prosthetic valve endocarditis, no.	0
• Prosthetic valve thrombosis, no.	0
• Repeat procedure for valve related dysfunction, no. (%)	
-SAVR[2], no. (%)	1 (3.7)
-Valve-in-valve, no. (%)	1 (3.7)
-Failure of current therapy for aortic regurgitation, no. (%)	1 (3.7)

- **All-cause mortality at 1 year – 20% with cardiovascular mortality – 10%**

Silaschi, et. al. , Catheter Cardiovasc Interv. 2018

J-valve

- Self-expanding Nitinol frame
- Porcine aortic valve
- Clasper—independently operated 3D ring that corresponds to the native sinuses, orients the valve stent, and captures the native leaflets
- Annular range: 19 – 27 mm
- 4 valve sizes: 21, 23,25, and 27 mm
- 27Fr sheathless transapical delivery catheter

J-valve

Trans-apical, severe AR, 33 patients,
mean age 74.2 ± 5.2, EuroSCORE 24.4 ± 5.1

Outcomes	
Device Success	94%
2nd Valve	0%
Conversion to SAVR	3%
30-Day Mortality	3%
Moderate / Severe PVL	3%
Permanent Pacemaker	6.10%

Zhu, et. al. , J Am Coll Cardiol 2016

Evolut R

- Self-expanding Nitinol frame
- Porcine pericardial supra-annular valve
- Optimized sealing: extended skirt and more conformable frame
- Recapturable
- Annular range: 18 – 30 mm
- 4 valve sizes: 23, 26, 29, 34 mm
- 14Fr –equivalent profile, vessels ≥ 5.0 mm
- 34 mm system: 16Fr-equivalent, vessels ≥ 5.5 mm

JenaValve Trilogy Heart Valve

- Self-expanding Nitinol frame
- Porcine pericardial tissue
- Locator clip onto native leaflets forming a natural seal
- Needs no calcium to anchor
- Less permanent pacemaker

- Annular range: 21 – 27 mm
  - 3 valve sizes: 23, 25, 27 mm
- Transfemoral access with an 18Fr profile

Accurate neo 2 THV

- Self-expanding Nitinol frame
- Porcine pericardial tissue
- Top-down deployment

- Annular range: 20 – 26.3 mm
  - 3 valve sizes
    - S: 20.0 – 22.4mm
    - M: 22.5 – 24.3mm
    - L: 24.4 – 26.3 mm
- Transfemoral access with an 18Fr profile

Accurate neo 2 THV

Pure non-calcified AR TAVR, total 9 patients, logEuroSCORE II 5.5 ± 3.6%, STS PROM 6.2 ±3.0%

	Study group (n = 9)
All-cause mortality (30 days), % (n)	0 (0)
Stroke (any), % (n)	0 (0)
Myocardial infarction, % (n)	0 (0)
Bleeding (major/life threatening), % (n)	0 (0)
Access site complications (major), % (n)	0.0 (0)
Acute kidney injury (AKIN* 2, 3), % (n)	22.2 (2)
PPM implantation, % (n)	0 (0)
Device success†, % (n)	100 (9)
Early safety‡, % (n)	77.7 (7)
Intensive care unit stay, days	1.7 ± 1.1
In hospital stay, days	12.9 ± 8.8
Peak gradient, mmHg	15.3 ± 12.3
Mean gradient, mmHg	7.2 ± 5.5
Mild PVL, % (n)	22.2 (2)
PVL > mild, % (n)	0 (0)

*PPM, Permanent pacemaker; PVL, Paravalvular leakage; *AKIN, Acute Kidney Injury Network; VARC-2 definitions: †Device success: absence of procedural mortality, correct positioning of a single prosthetic heart valve into the proper anatomical position, intended performance of the prosthetic heart valve (no prosthesis-patient mismatch and mean aortic valve gradient < 20 mmHg or peak velocity < 3 m/s and no moderate or severe prosthetic valve regurgitation), ‡Early safety at 30 days: all-cause mortality (at 30 days), all stroke (disabling and non-disabling), life-threatening bleeding, acute kidney injury stage 2 or 3 (including renal replacement therapy), coronary artery obstruction requiring intervention, major vascular complication, valve-related dysfunction requiring repeat procedure (Balloon aortic valvuloplasty, TAVI, or SAVR).*

TAVR for pure native AR

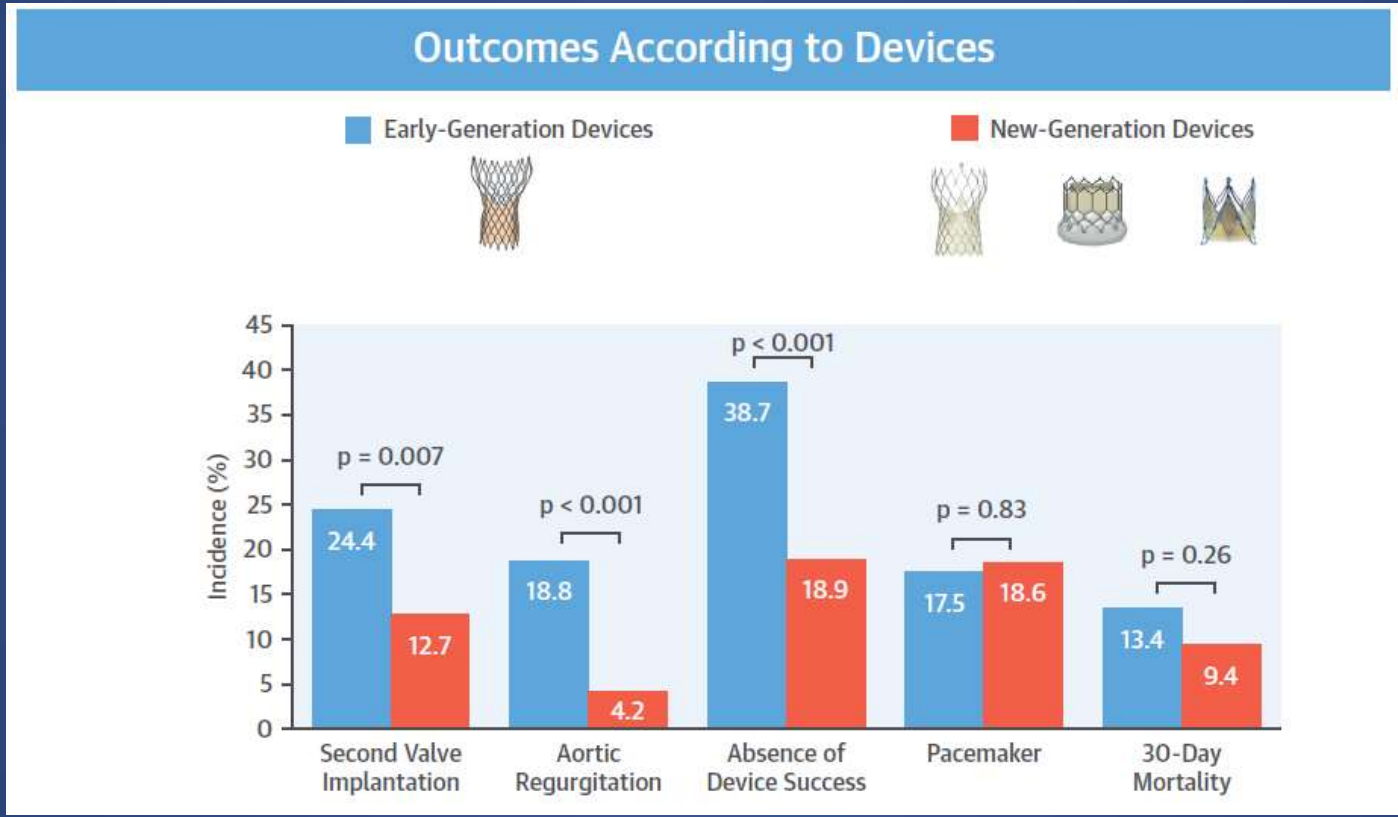
Pure native AR TAVR multicenter registry, total 331 patients, STS score 6.7 ±6.7

	Overall (N = 331)	Early-Generation Devices (n = 119)	New-Generation Devices (n = 212)
Device type			
Sapien XT	9 (2.7)	9 (7.6)	–
Sapien 3	41 (12.4)	–	41 (19.3)
CoreValve	110 (33.2)	110 (92.4)	–
Evolut R	50 (15.1)	–	50 (23.6)
JenaValve	64 (19.3)	–	64 (30.2)
Direct Flow	35 (10.6)	–	35 (16.5)
J-Valve	1 (0.3)	–	1 (0.5)
Engager	7 (2.1)	–	7 (3.3)
Portico	3 (0.9)	–	3 (1.4)
Acurate	5 (1.5)	–	5 (2.4)
Lotus	6 (1.8)	–	6 (2.8)

Sung-Han Yoon, et al. JACC 2017

TAVR for pure native AR

Pure native AR TAVR multicenter registry, total 331 patients, STS score 6.7 ±6.7

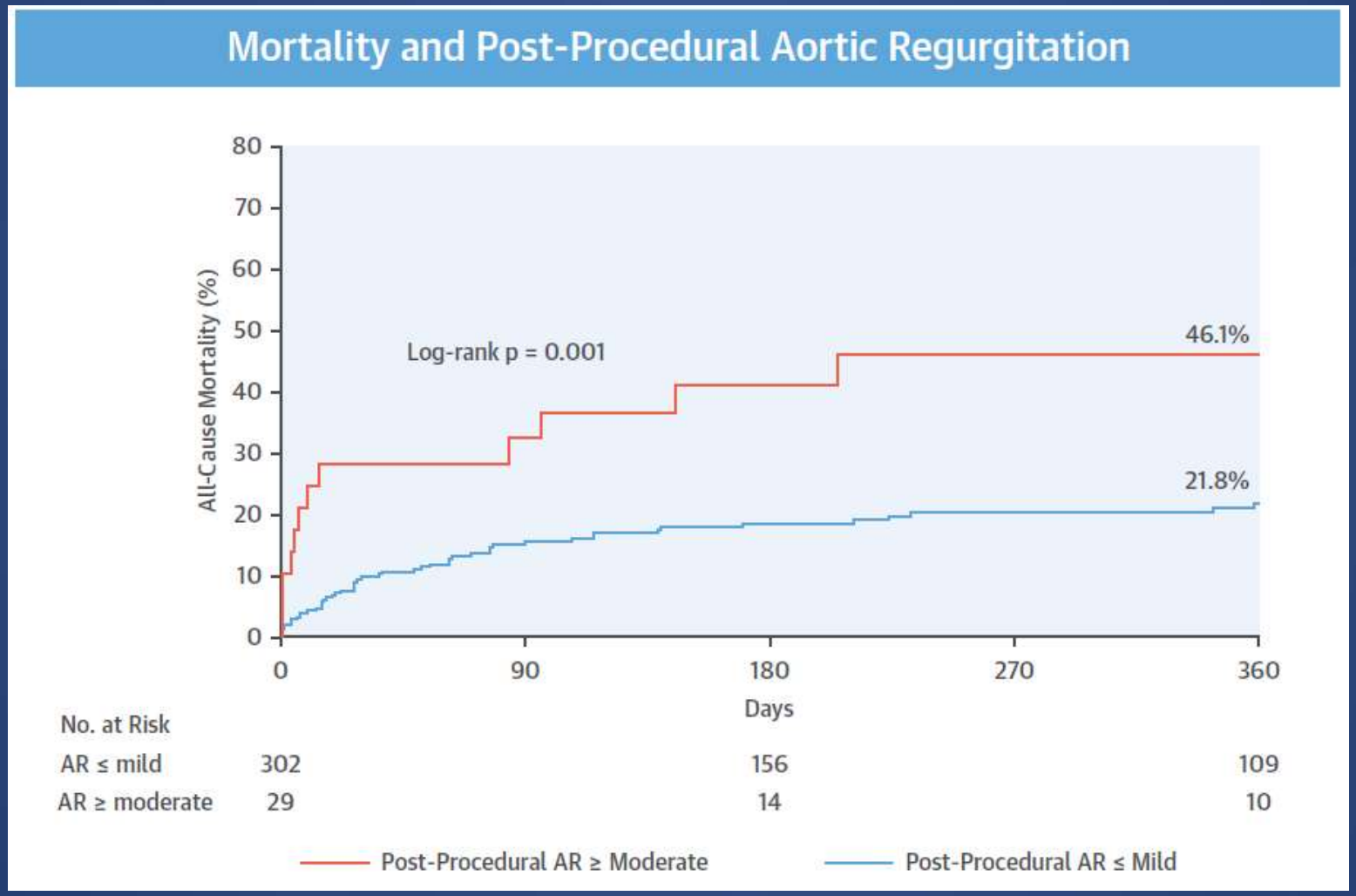


Implications: High-risk or inoperable patients who undergo TAVR to treat pure native AR fare better when they receive new- vs early-generation valves.

Sung-Han Yoon, et al. JACC 2017

TAVR for pure native AR

Pure native AR TAVR multicenter registry, total 331 patients, STS score 6.7 ±6.7



Sung-Han Yoon, et al. JACC 2017

Pure AR in native and prosthetic valve

78 patients with native valve / 68 patients with prosthetic valve

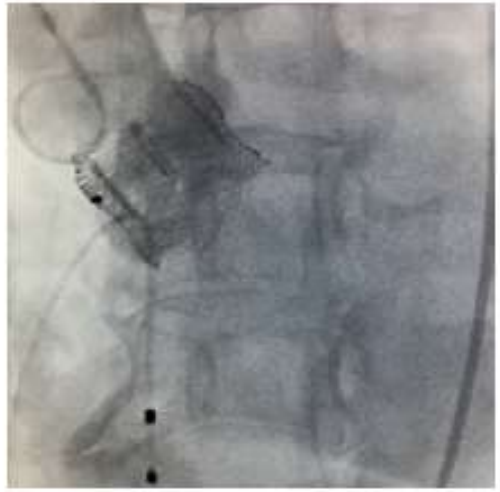
	Pure Severe NAVR (n = 78)	Failing SHV With Severe AR (n = 68)
THV device		
CoreValve	33/78 (42%)	38/68 (56%)
Evolut R	5/78 (6%)	7/68 (10%)
JenaValve	23/78 (29%)	–
Direct Flow	6/78 (8%)	1/68 (1%)
Lotus	6/78 (8%)	–
SAPIEN XT	4/78 (5%)	17/68 (25%)
SAPIEN 3	1/78 (1%)	5/68 (7%)

Fadi J. Sawaya, et al. JACC intv 2017

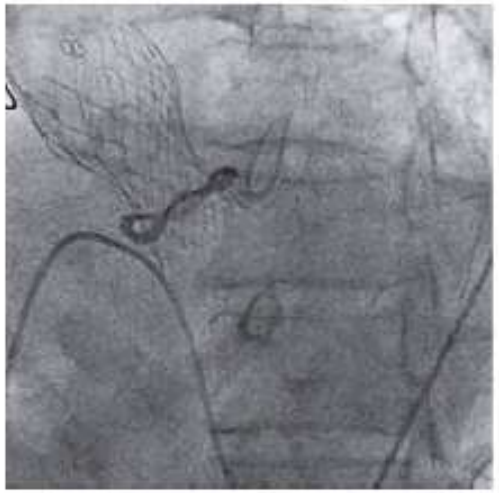
Pure AR in native and prosthetic valve

78 patients with native valve / 68 patients with prosthetic valve

Native aortic valve regurgitation (NAVR)



Failing surgical heart valve (SHV)



Old-Gen THV	New-Gen THV		Old-Gen THV	New-Gen THV
54%	85%	**Device success**	69%	77%
62%	69%	**Early safety**	90%	92%
46%	75%	**Clinical efficacy**	77%	77%

Fadi J. Sawaya, et al. JACC intv 2017

TAVR in AR : The U.S. experience

Study cohorts from Nationwide Inpatient Sample (NIS) and Nationwide Readmissions Database (NRD), 2016-2017
915 patients from NIS, 822 patients from NRD

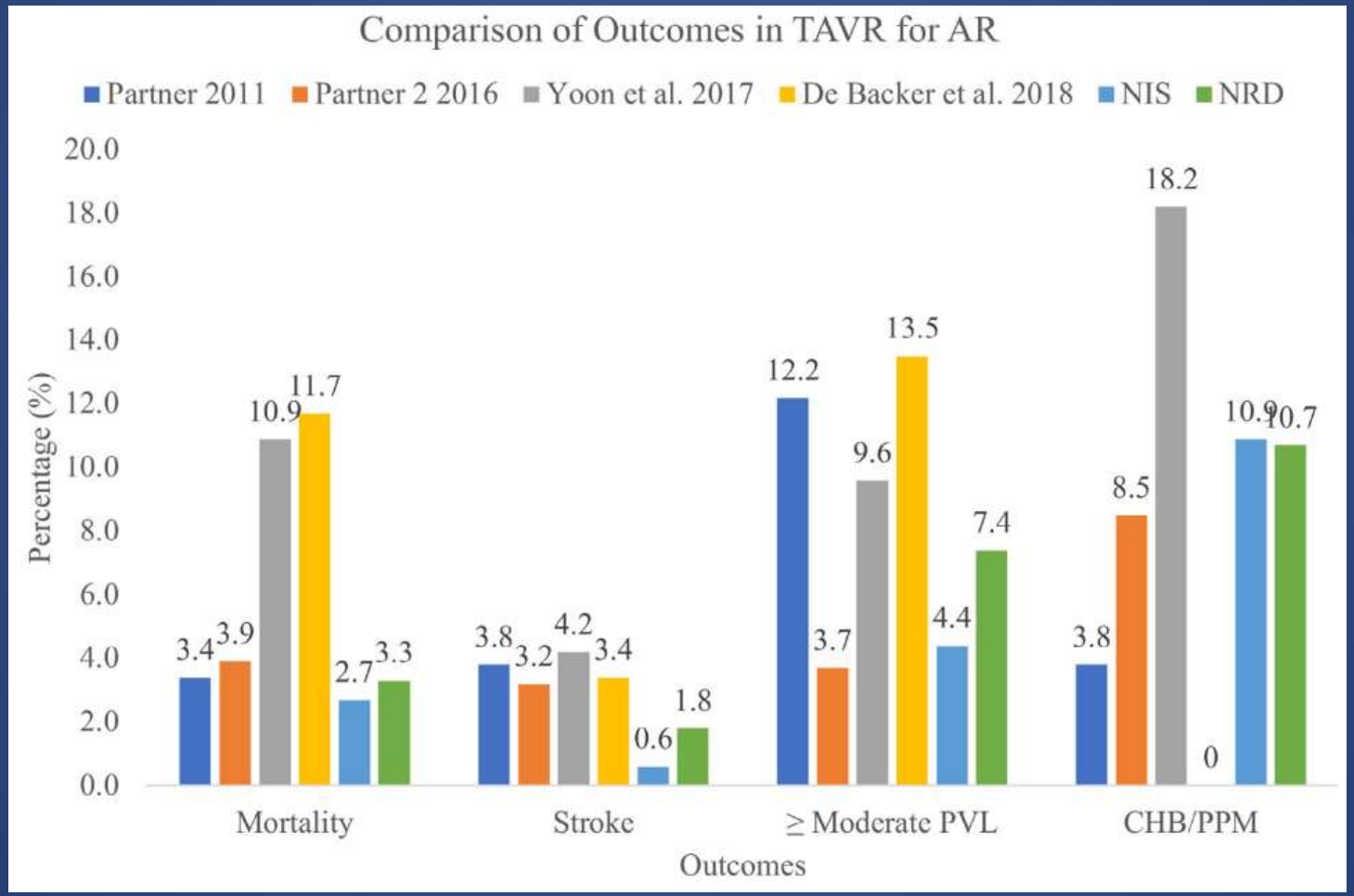
TABLE 2 Complications associated with TAVR in AR

TAVR in AR	NIS In-hospital complications	NRD 30-day complications
Patient population	915	822
Overall complications	38.3	39.9
All-cause mortality	2.7	3.3
Disabling stroke	0.6	1.8
Valvular complications	19.1	18.2
Moderate to severe para-valvular regurgitation	4.4	7.4
Displacement of valve	0.6	0.2
Infection of valve	0.0	1.2
Breakdown of valve	4.4	5.2
Unspecified valve complications	9.8	9.3
Complete heart block/permanent pacemaker placement	10.9	10.7
Open heart surgery for aortic valve	0.0	0.6
Acute kidney injury needing hemodialysis	0.0	2.2
Acute myocardial infarction	6.0	4.6
Periprocedural shock	1.6	0.7
Any pericardial complications	1.6	0.9
Transient ischemic attack	0.0	0.3
Major bleeding need transfusion	2.2	7.7
Vascular complications	1.1	1.5

Arora, et al. Catheter Cardiovasc. Interv 2021

TAVR in AR : The U.S. experience

Study cohorts from Nationwide Inpatient Sample (NIS) and Nationwide Readmissions Database (NRD), 2016-2017
915 patients from NIS, 822 patients from NRD



Arora, et al. Catheter Cardiovasc. Interv 2021

The ALIGN-AR EFS Trial : JenaValve Pericardial TAVR AR

Transfemoral JenaValve Pericardial TAVR in patients with severe AR

- NCT02732704
- Primary outcome: All-cause mortality at 30 days,
- Secondary outcome: Mortality, Peri-procedural MI, Stroke-Free survival, Bleeding & Vascular complications

The JenaValve ALIGN-AR Pivotal Trial (ALIGN-AR)

To assess safety and effectiveness of the JenaValve Trilogy in high surgical risk patients with severe AR

- NCT04415047
- On recruiting
- Primary outcome: All-cause mortality at 1 Year, All stroke, Major bleeding, AKI, Major vascular complications, Surgery/intervention related to the device, PPM, total AR
- Secondary outcome: KCCQ improvement

TAVR

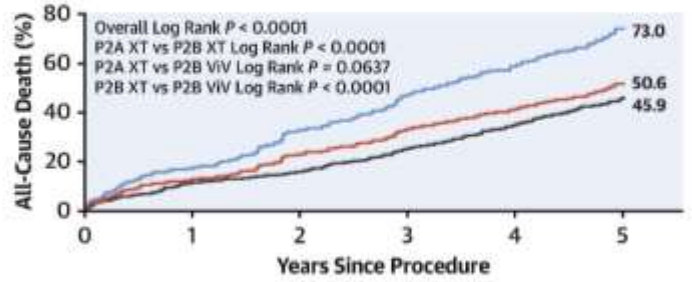
Valve-in-Valve

PARTNER 2 Valve-in-Valve Registry

5-year outcomes

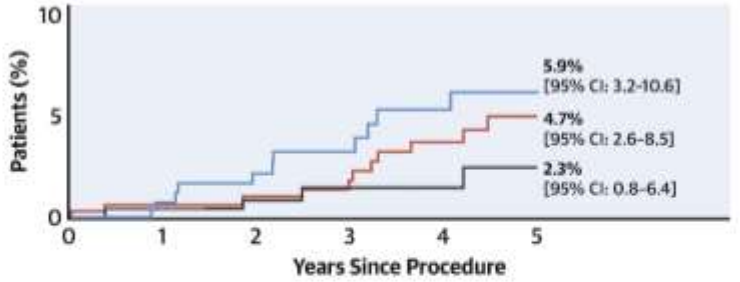
Transcatheter Valve-in-Valve (ViV) 5-Year Outcomes in High Surgical Risk Patients

A



No. at risk:						
— P2B XT (Inoperable)	280	217	177	147	111	46
— P2B XT ViV (High Risk)	365	320	274	234	190	141
— P2A XT (Intermediate Risk)	974	854	800	696	592	311

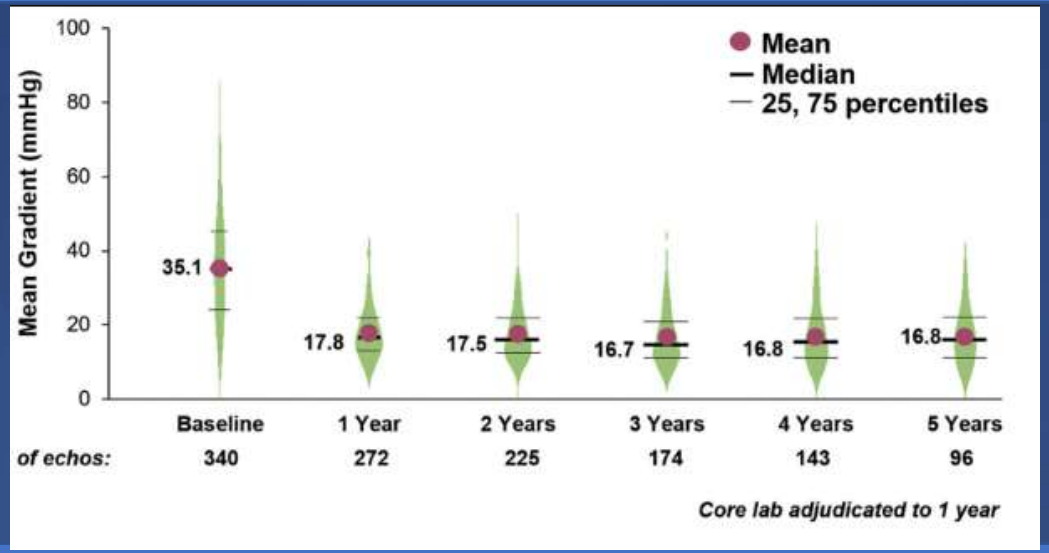
B



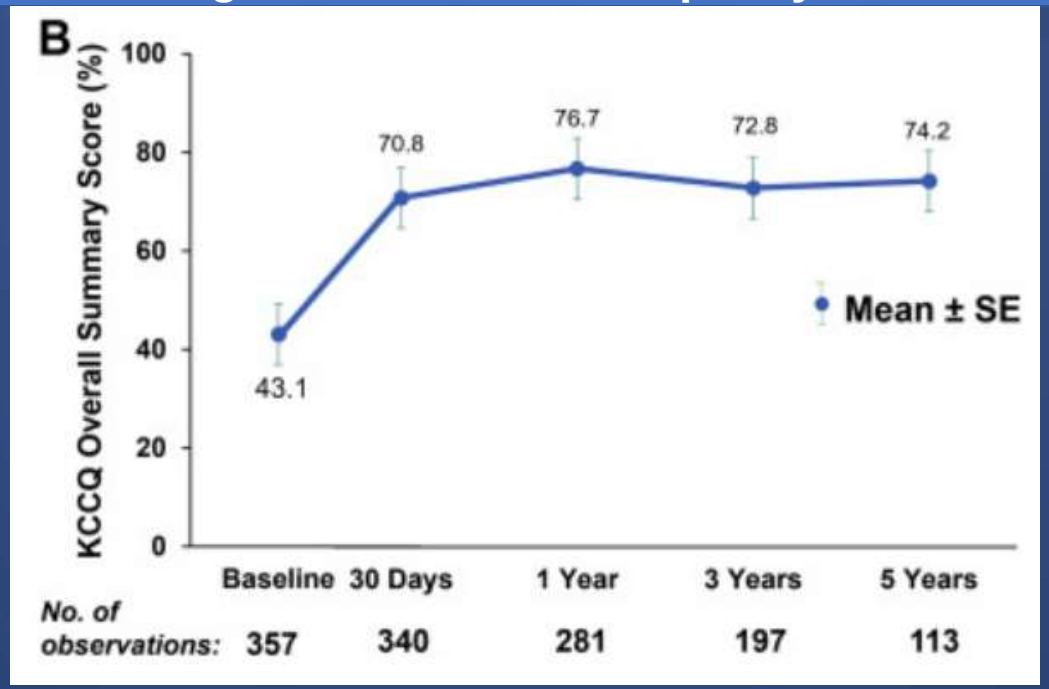
No. at risk:						
— SVD-Related HVD	273	251	201	158	125	86
— All BVF	365	319	272	231	185	137
— SVD-Related BVF	273	253	205	162	131	92

Hahn RT, et al. J Am Coll Cardiol Intv. 2022;15(7):698-708.

A. Changes in hemodynamics



B. Changes in function and quality of life



Hahn RT, et al., JACC Cardiovasc Interv. 2022 Apr 11;15(7):698-708.

Hemodynamic Deterioration of Surgically Implanted Bioprosthetic Aortic Valves

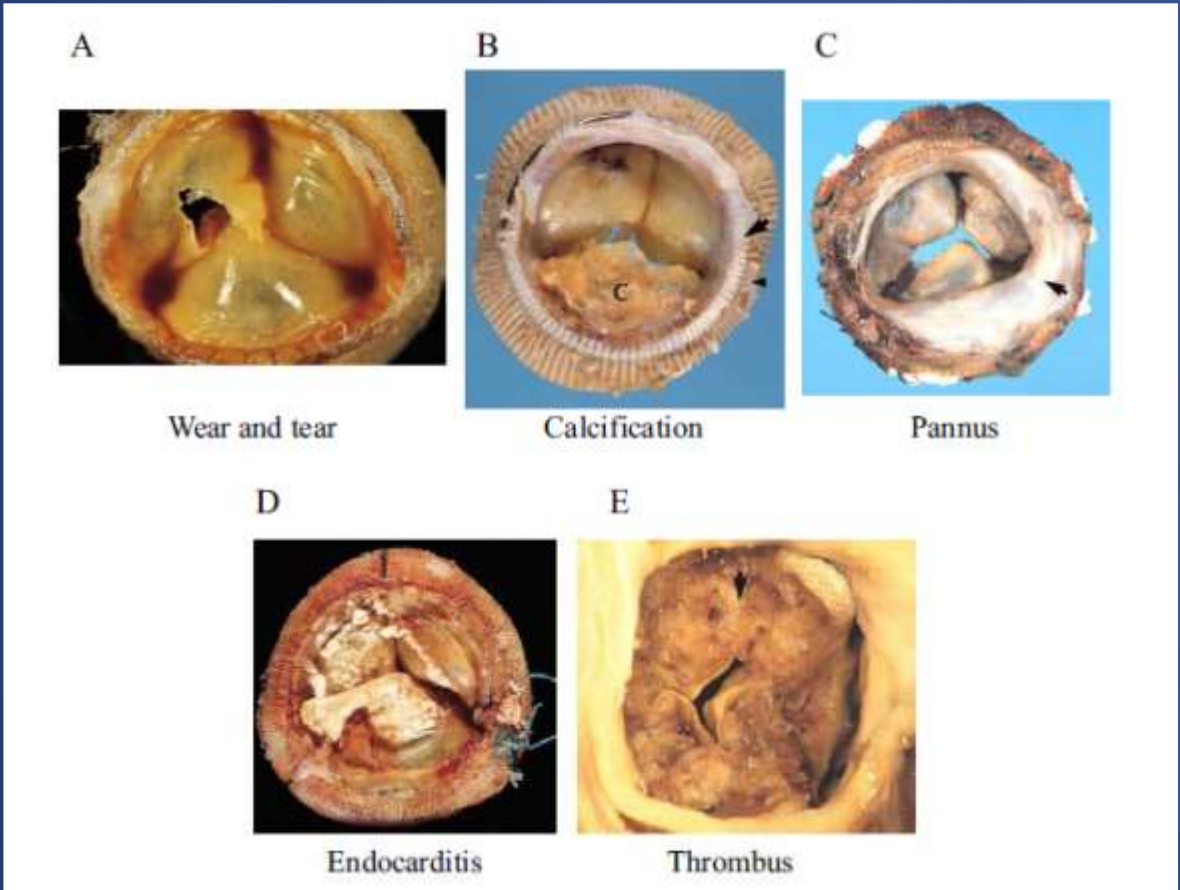
Prospective longitudinal study of 137 patients who had previously undergone bioprosthetic valve surgery.

- 25.6% had leaflet calcification on noncontrast CT at a median of 6.7 years post-SAVR. By a median of 3 years later, 13.1% of pts developed hemodynamic valve deterioration (HVD)
- Leaflet calcification independently predicted the risk of death/reintervention (HR 2.58; 95% CI 1.35-4.82), as did HVD (HR 5.12; 95% CI 2.57-9.71)
- Predictors of HVD were leaflet calcification, insulin resistance, increased Lp-PLA2 activity, and high PCSK9 level

Implications: Dysmetabolic profile and calcification could be early warning signs of hemodynamic deterioration of bioprosthetic valves.

Salaun E, et al. J Am Coll Cardiol. 2018;72:241-251.

Most Common Reasons for Bioprosthetic Valve Failure



(A) Wear and tear

(B) Calcific degeneration

(C) Pannus

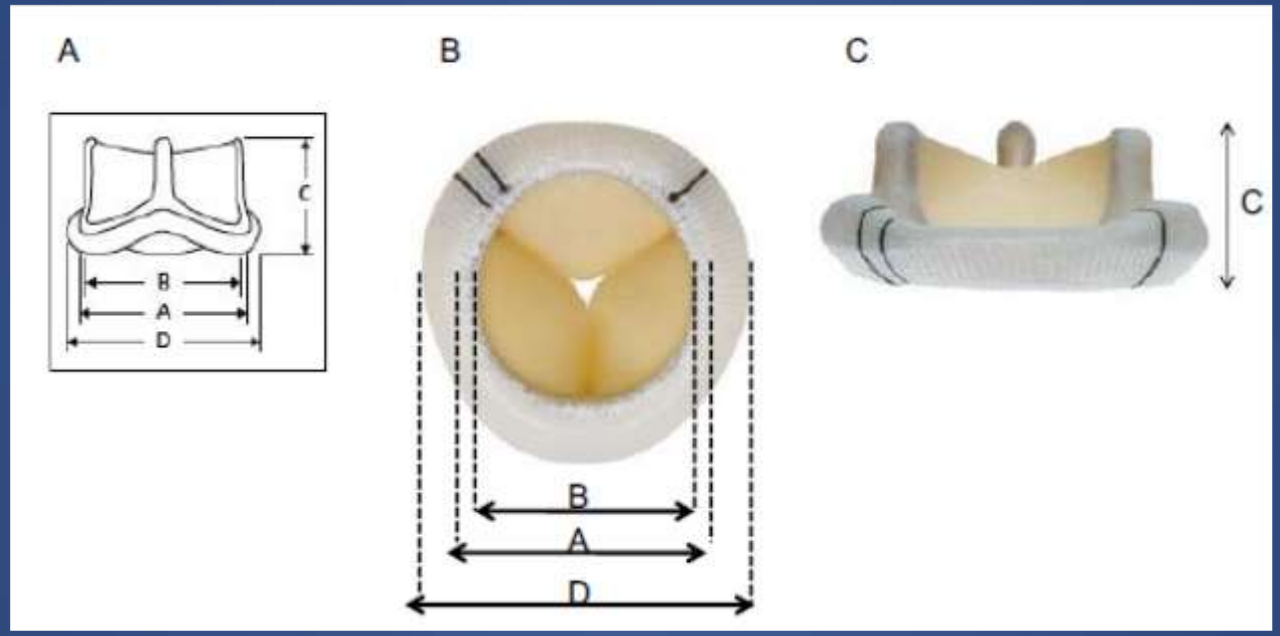
(D) Endocarditis

(E) Thrombus

Wear and tear (A) and calcification (B) are the most common reasons for bioprosthetic valve failure

Piazza, N, et al. JACC Cardiovasc Interv. 2011;4:721-32.

Dimensions of Stented Bioprosthetic Valves



(A) Diagrammatic representation of stented bioprosthetic valve dimensions
A outer stent diameter
B inner stent diameter
C prosthesis height
D outer sewing ring diameter.

(B) Inferior (ventricular) view of stented bioprosthesis.

(C) Side view of stented bioprosthesis.

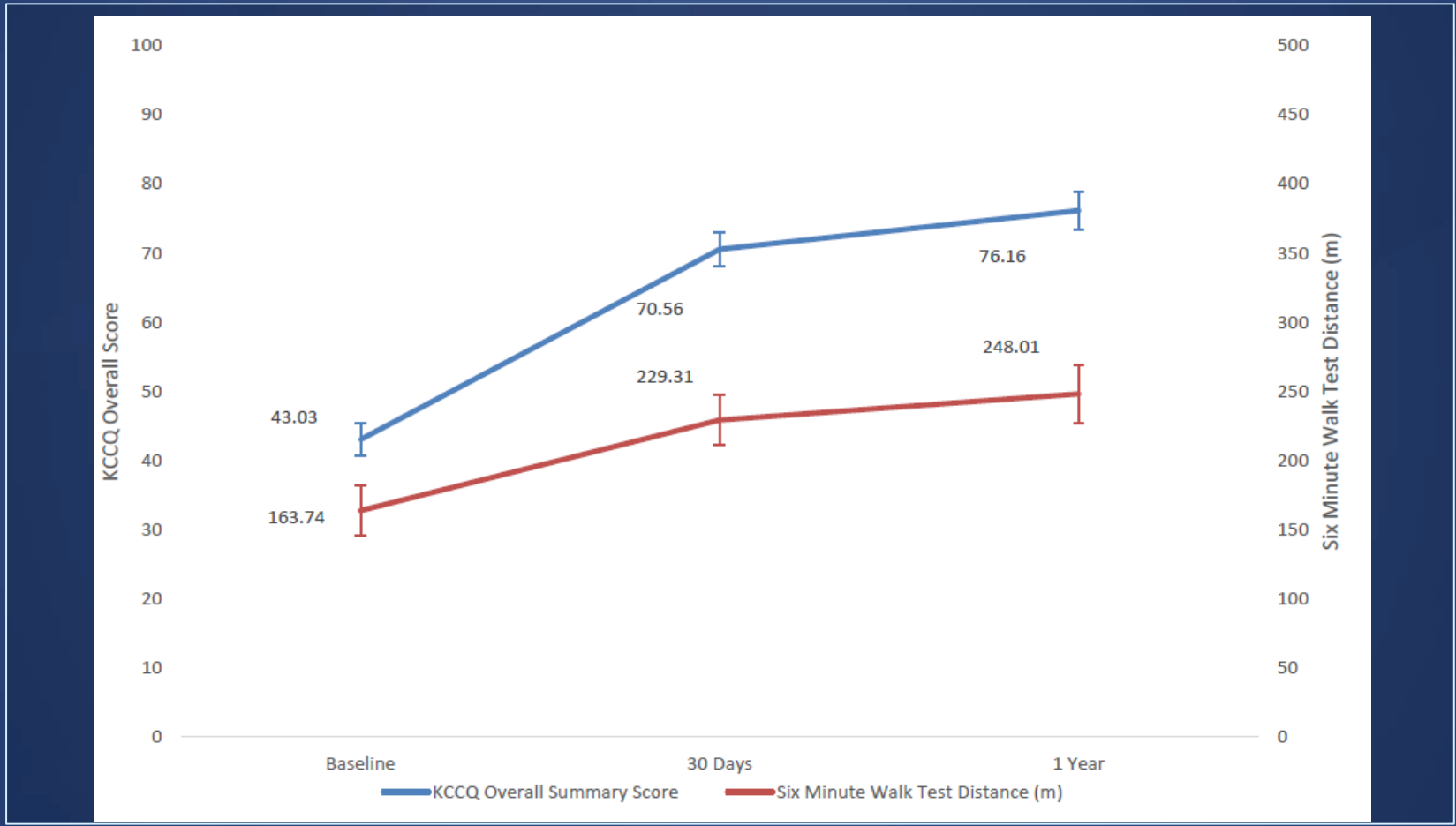
Piazza, N, et al. JACC Cardiovasc Interv. 2011;4:721-32.

TAVR for degenerative bioprosthetic surgical valves: Valve-in-Valve Registry

- **Treating a failed bioprosthesis via TAVR**
  Feasible and often effective but technically demanding
- **The Global Valve-in-Valve Registry**
  - 416 high-risk patients
  - 54 centers in Europe, North America, Australia, New Zealand, and the Middle East
  - 225 Sapien (Edwards) /190 CoreValve /1 Melody (Medtronic)
- **"Relatively high rates" of Complications**
  - initial device malapposition / attempted valve retrieval
  - implantation of a second device
  - post-implantation valvuloplasty
  - need for emergent surgery
  - clinically-evident coronary obstruction
- **Improvement of functional capacity at 30 days**
  87.5% of patients classified as NYHA class I/IIs

Danny Dvir, MD, Washington Heart Center

Aortic Valve-in-Valve is an effective procedure



PARTER NR3 viv. JACC 2017

TAVR for degenerative bioprosthetic surgical valves

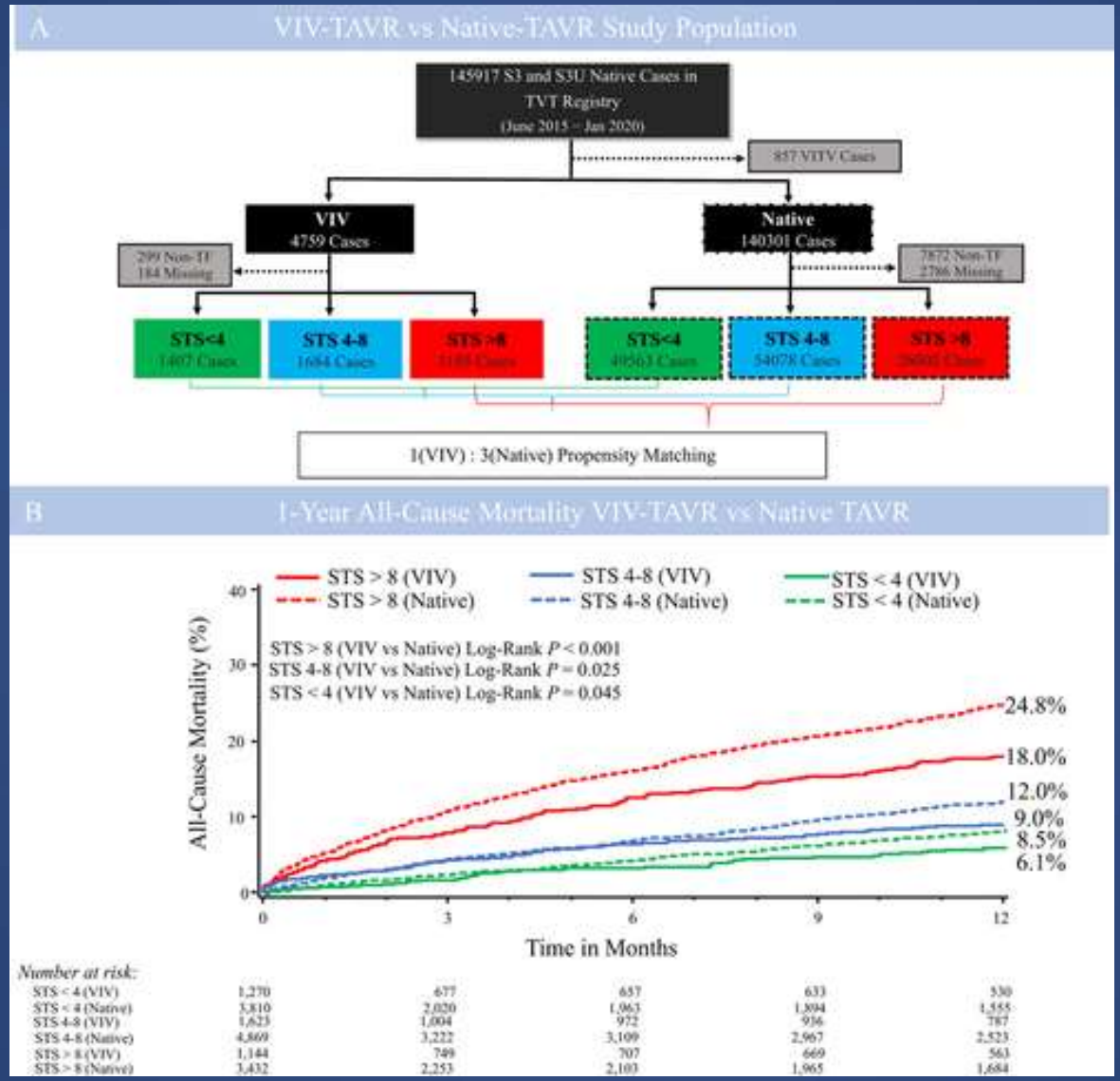
Valve-in-Valve Registry

Mortality at 30 Days				
	Mechanism of bioprosthetic valve failure			
	Stenosis (n = 168)	Regurgitation (n = 125)	Combined (n = 123)	*P* Value
All-Cause	10.9%	4.1%	6.7%	0.09
Cardiovascular	9.8%	3.3%	5.8%	0.08

- Registry shows valve-in-valve procedure via TAVR can effectively treat failed bioprostheses
- Poorest outcomes seen in patients with stenosis vs regurgitation or combination of both
- Technically challenging procedure best performed by experienced operators

Danny Dvir, MD, Washington Heart Center

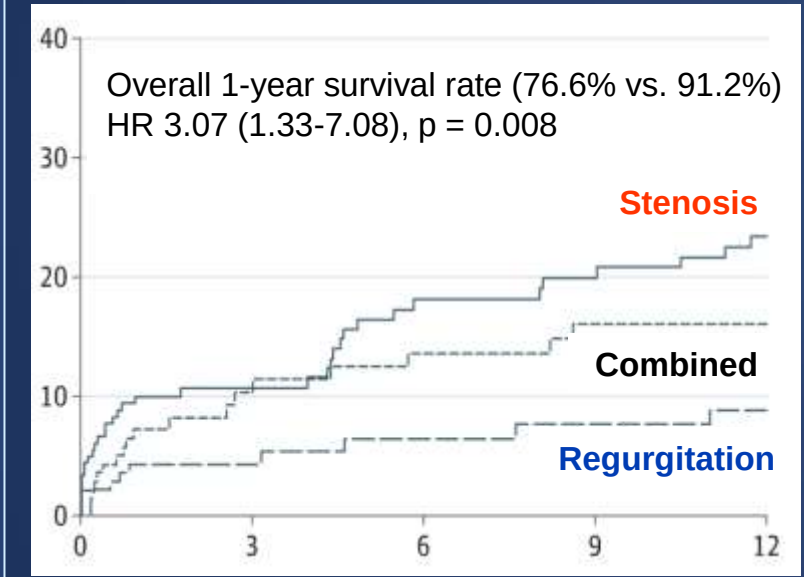
Valve-In Valve TAVR



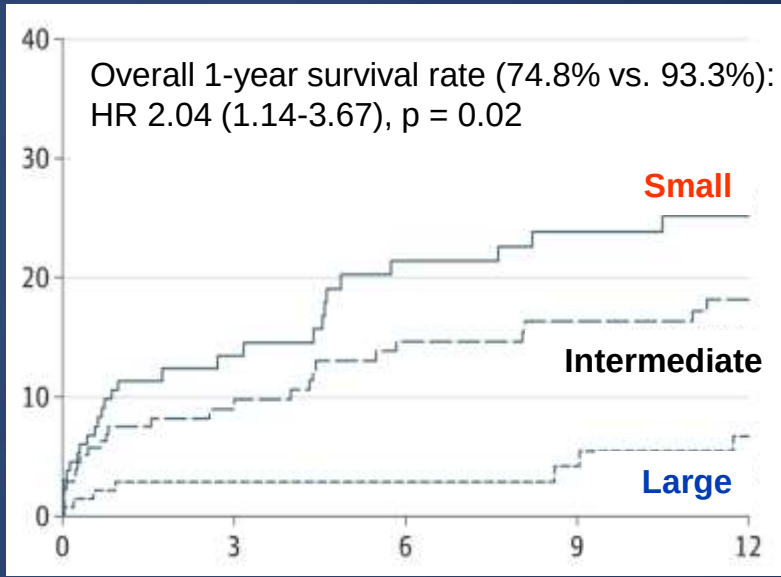
Kaneko T, et al., Circ Cardiovasc Interv. 2021 May;14(5)

Valve-In Valve TAVR

Predominant Bioprostheses
Stenosis vs. Regurgitation



Size of Bioprostheses
Small vs. Large



A total of 459 patients with degenerated bioprosthetic valves undergoing valve-in-valve were evaluated.

Dvir D et al. JAMA. 2014;312(2):162-170

30-day Outcomes of Valve-in-Valve

Stenosis vs. Regurgitation

Outcomes	All N = 459	Stenosis N = 181	Regurgitation N = 139	Combined N = 139
30 day mortality, %				
All-cause	7.6	10.5	4.3	7.2
Cardiac cause	6.5	8.8	3.6	6.5
Major Stroke, %	1.7	0.6	2.2	2.9
Major vascular complications, %	9.2	7.7	7.2	12.9
Life threatening/major bleeding, %	8.1	11.0*	3.6*	8.6*
Acute kidney injury (stage II/III), %	7.4	8.8	7.2	5.8
New permanent pacemaker, %	8.3	9.4	8.6	6.5
Aortic regurgitation ≥moderate, %	5.4	2.8*	9.4*	5.0*
Ejection fraction %	52±12	54±10*	49±12*	51±13*

* p value < 0.05

1-year Outcomes of Valve-in-Valve

Stenosis vs. Regurgitation

Outcomes	All N = 459	Stenosis N = 181	Regurgitation N = 139	Combined N = 139
1-year mortality, %	16.8	23.4	8.8	16.1
NYHA class III/IV, %	13.8	15.1	14.8	11.3
AV area, cm2	1.4±0.4	1.3±0.3*	1.5±0.5*	1.4±0.5*
AV peak gradient, mm Hg	30±15*	32±15*	25±15*	32±13*
AV mean gradient, mm Hg	17±9	18±10	14±9	18±8

* p value < 0.05

30-day Outcomes of Valve-in-Valve

SAPIEN vs. CoreValve

Outcomes	All N = 459	Sapien N = 246	CoreValve N = 213	p value
30day-mortality, %				
All-cause	7.6	8.1	7.0	0.66
Cardiac cause	6.5	7.3	5.6	0.47
Major Stroke, %	1.7	2.4	0.9	0.22
Major vascular complications, %	9.2	10.6	7.5	0.26
Life threatening/major bleeding, %	8.1	11.0	4.7	0.01
Acute kidney injury (stage II/III), %	7.4	10.2	4.2	0.02
New permanent pacemaker, %	8.3	4.9	12.2	0.05
Aortic regurgitation ≥moderate, %	5.4	2.4	8.9	0.002
Ejection fraction %	52±12	52±11	51±12	0.002

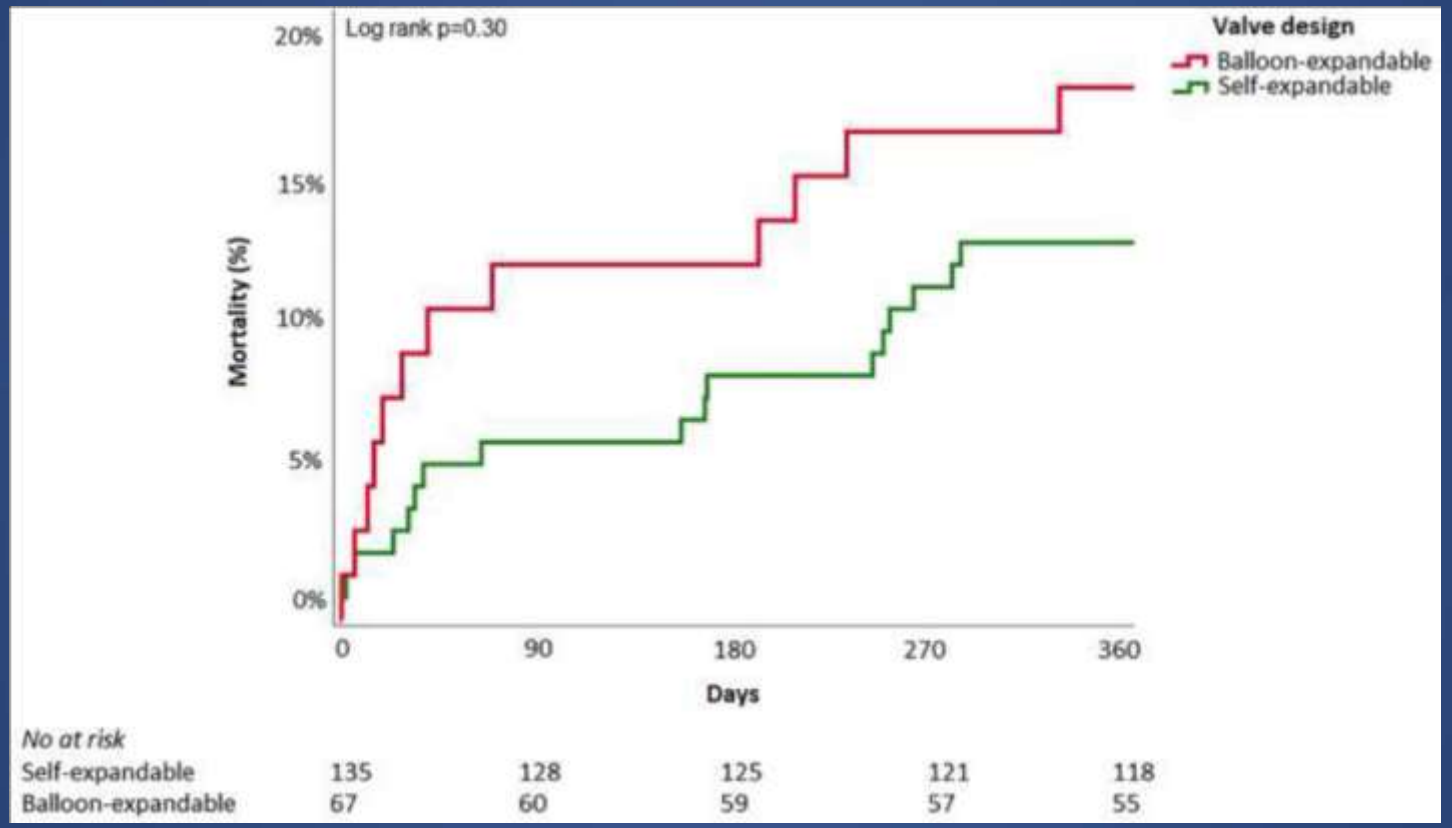
1-year Outcomes of Valve-in-Valve

SAPIEN vs. CoreValve

Outcomes	All N = 459	Sapien N = 246	CoreValve N = 213	p value
1-year mortality, %	16.8	15.0	18.7	0.44
NYHA class III/IV, %	13.8	18.4	17.6	0.89
AV area, cm2	1.4 ± 0.4	1.6 ± 0.4	1.3 ± 0.4	0.006
AV peak gradient, mm Hg	30 ± 15*	25 ± 12	33 ± 16	< 0.001
AV mean gradient, mm Hg	17 ± 9	14 ± 7	19 ± 10	< 0.001

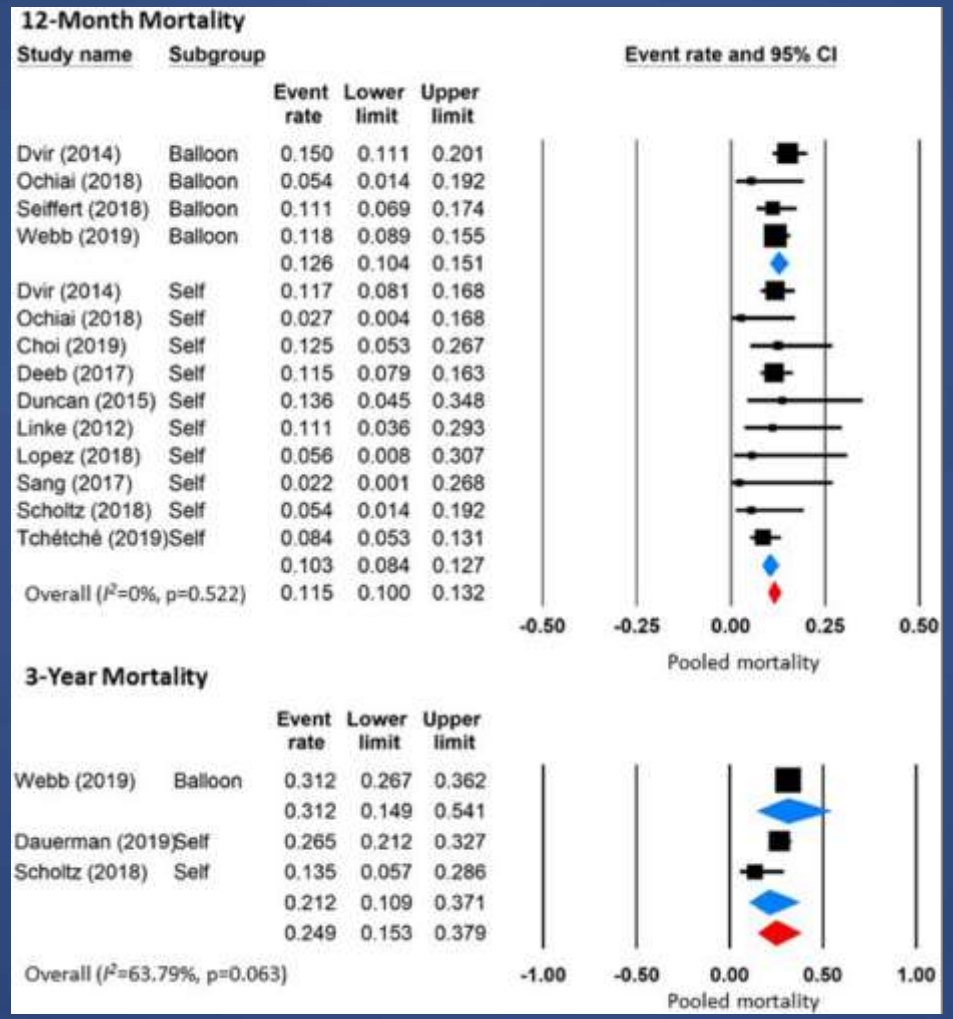
* p value < 0.05

Balloon-expandable vs. Self-expandable outcome in Valve-in-Valve



van Nieuwkerk AC.et al. Am J Cardiol. 2022 Jun 1;172:81-89

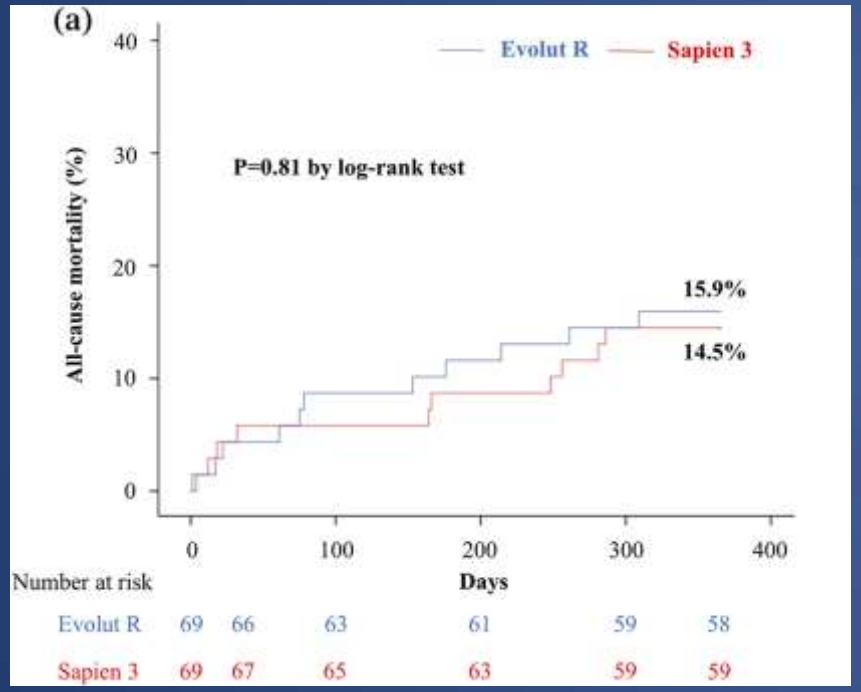
Balloon-expandable vs. Self-expandable outcome in Valve-in-Valve



Hamilton GW, et al., Am J Cardiol. 2020 May 15;125(10):1558-1565.

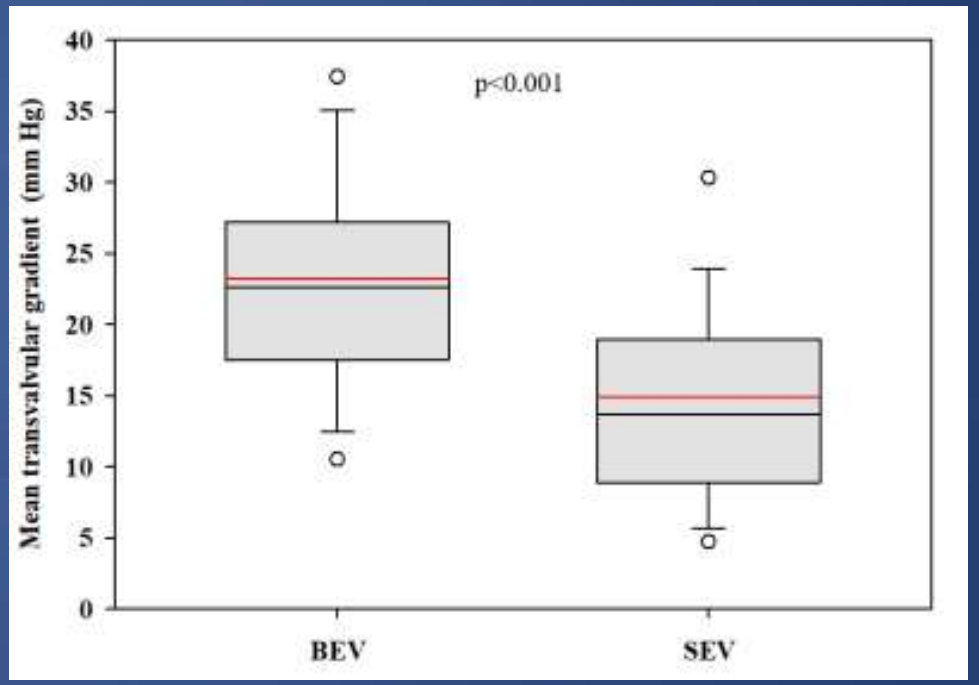
Balloon-expandable vs. Self-expandable In small aortic annulus (≤23mm)

All-cause mortality



Hase H, et al., The OCEAN-TAVI registry. Catheter Cardiovasc Interv. 2021 May 1;97(6):E875-E886.

Mean PG by echocardiography after 30day of procedure

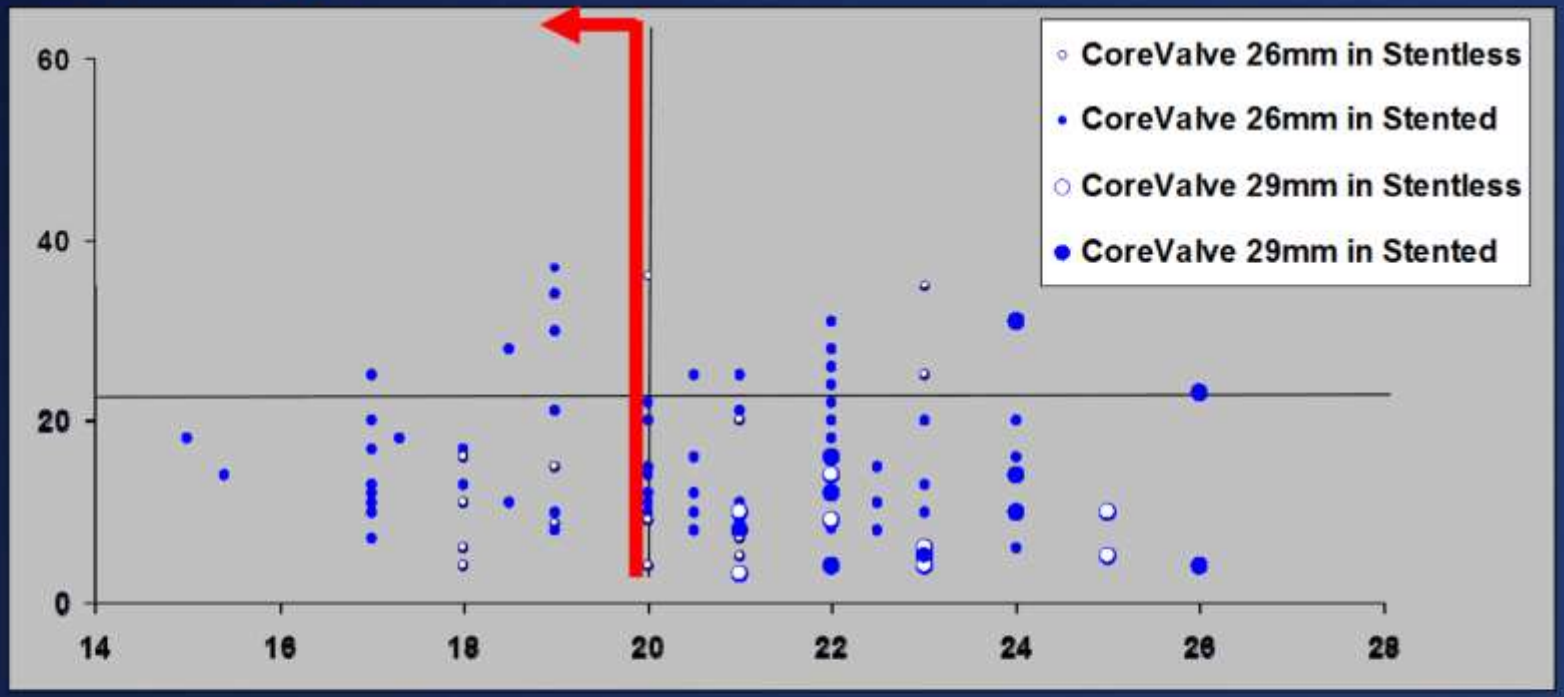


Rodés-Cabau J, et al., The LYTEN Trial. J Am Coll Cardiol. 2022 May 13:S0735-1097(22)04978-6.

Post Procedural Gradients

CoreValve Device

Mean Aortic-Valve Gradients (mmHg)



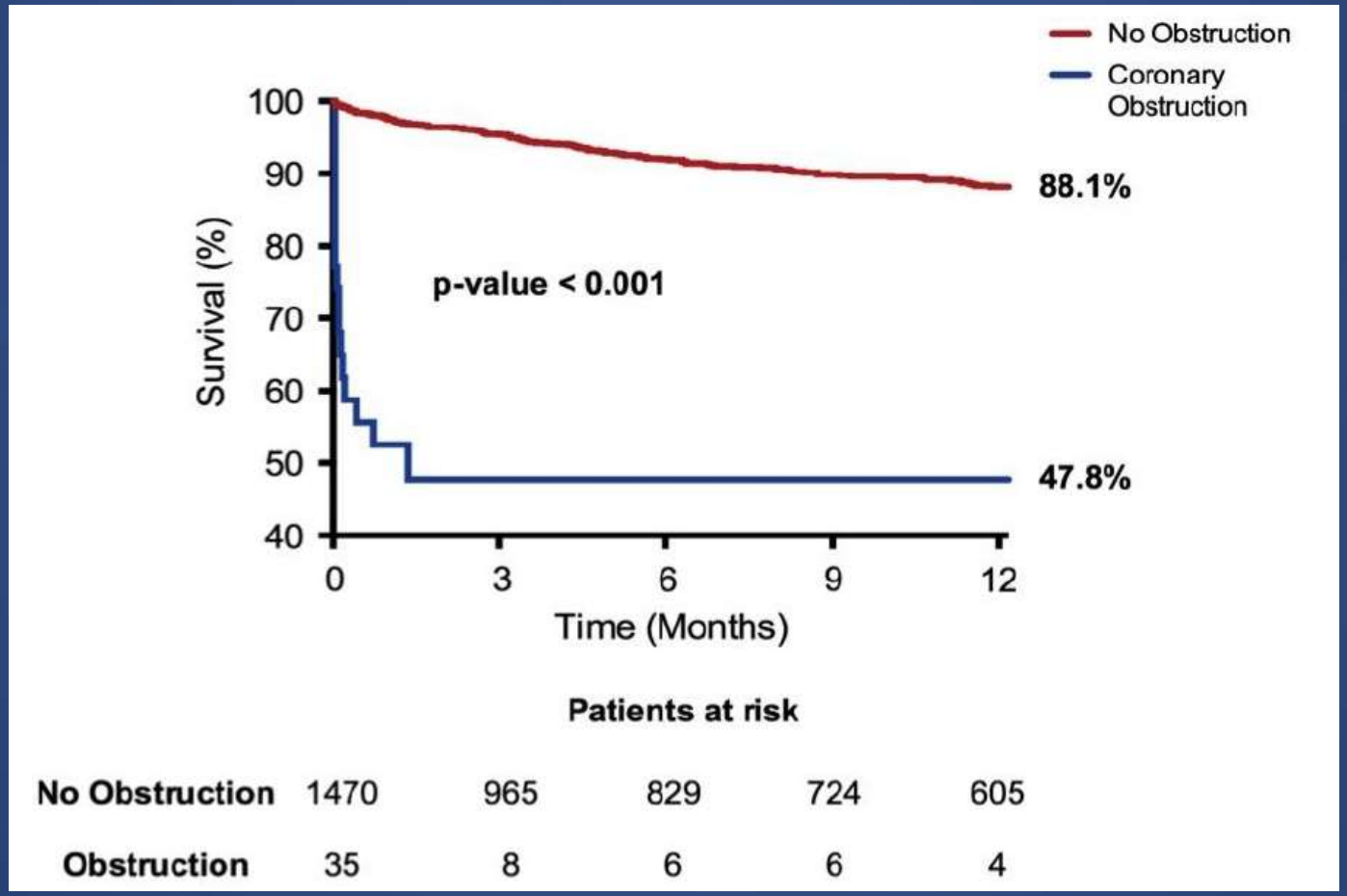
Surgical Bioprosthesis *Internal* Diameter (mm)

In small surgical bioprosthesis (<20mm ID)- 25.9% had elevated gradients

1. Divir, D. Global Valve Registry. TCT 2011.

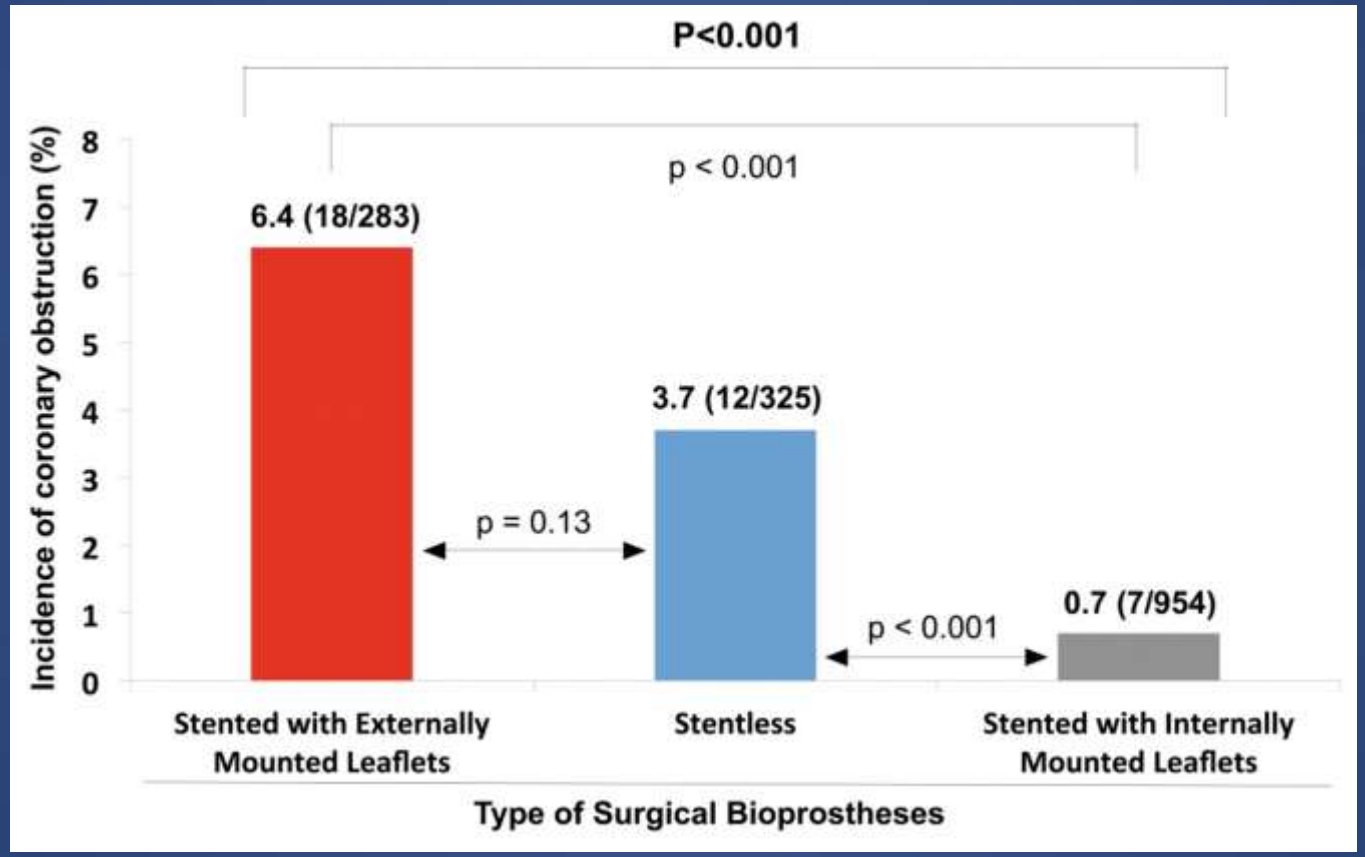
* Mean aortic-valve gradient> 20mmHg.

Coronary Obstruction after Valve-in-Valve procedure



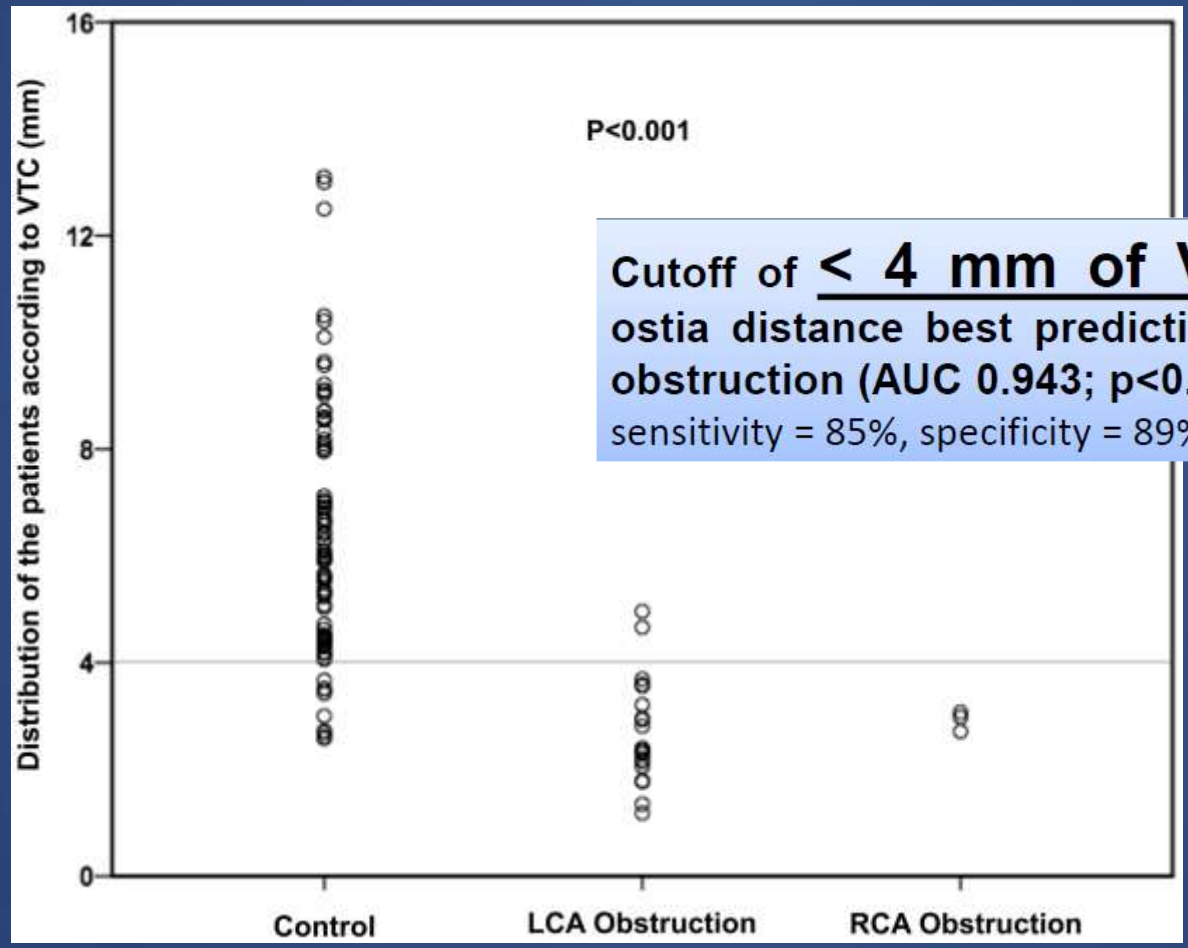
Ribeiro HB et al. TCT 2016

Incidence of Coronary Obstruction According to the Type of Surgical Bioprosthesis



Ribeiro HB, et al., Eur Heart J. 2018 Feb 21;39(8):687-695

Distribution of the Patients According to VTC-LCA Ostia Distance (mm)

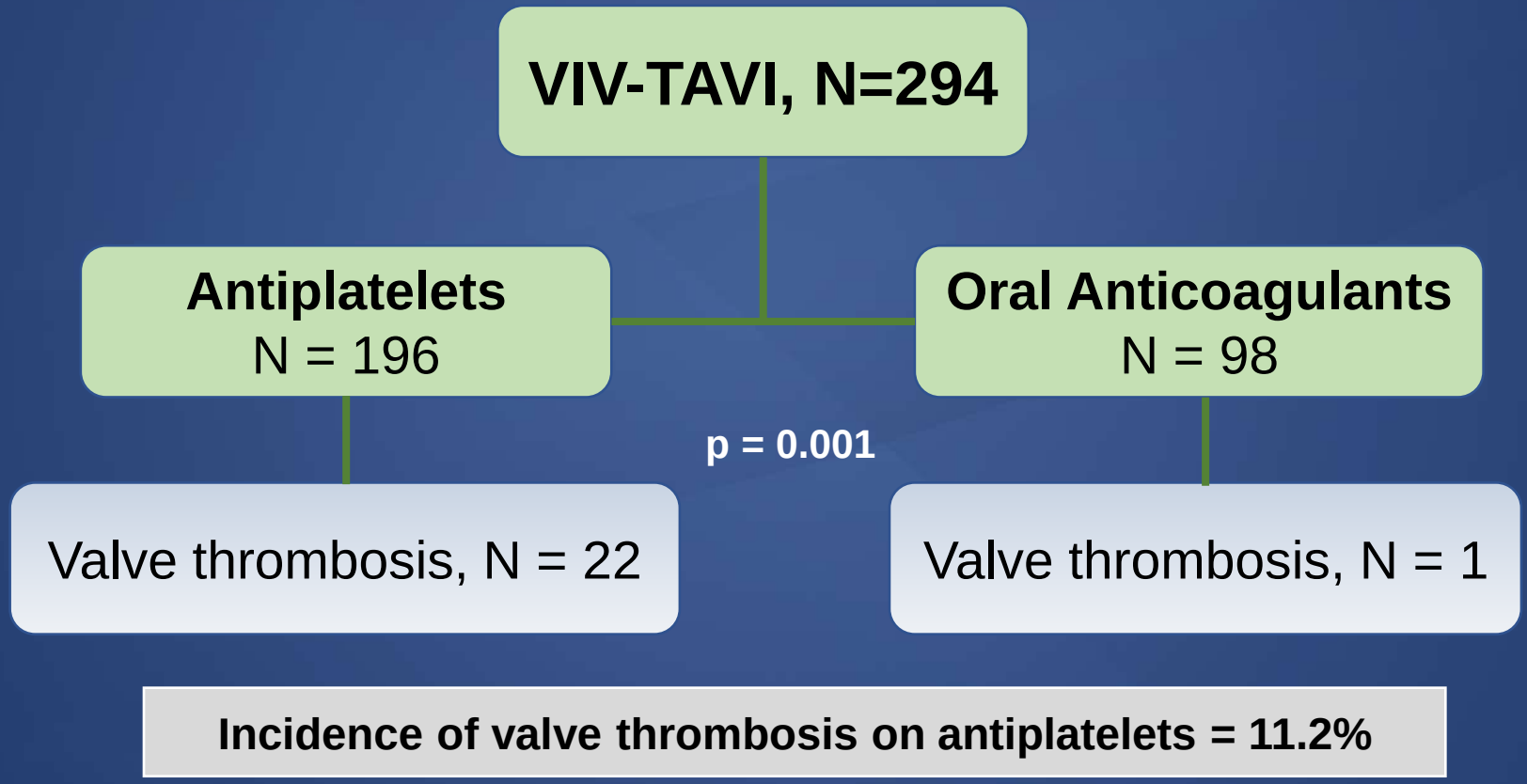


Cutoff of < 4 mm of VTC-LCA ostia distance best predicting coronary obstruction (AUC 0.943; p<0.001)
sensitivity = 85%, specificity = 89%

Ribeiro HB, et al., Eur Heart J. 2018 Feb 21;39(8):687-695

Thrombosis after aortic VinV

Incidence of valve thrombosis

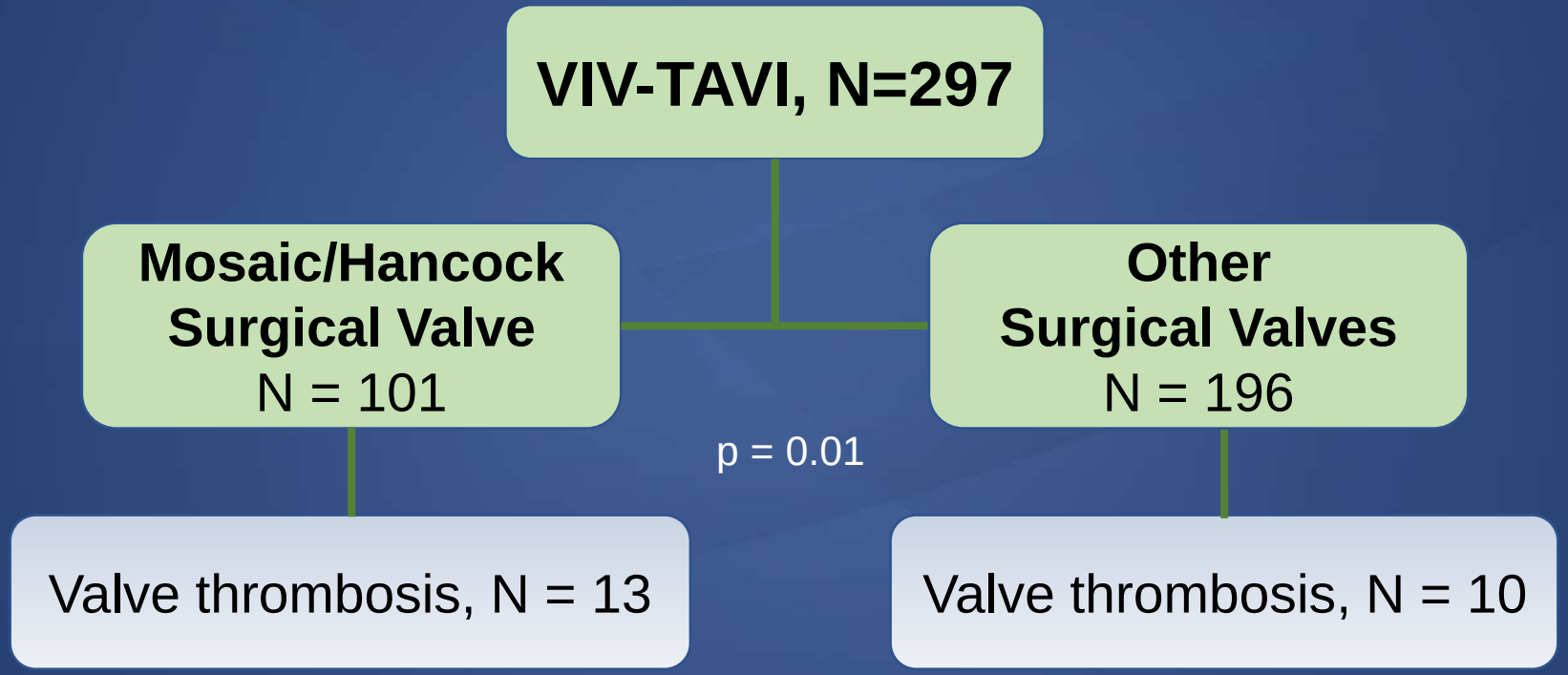


Incidence of valve thrombosis on antiplatelets = 11.2%

Danny Dvir, MD. TVT 2017

Thrombosis after aortic VinV

Incidence of valve thrombosis



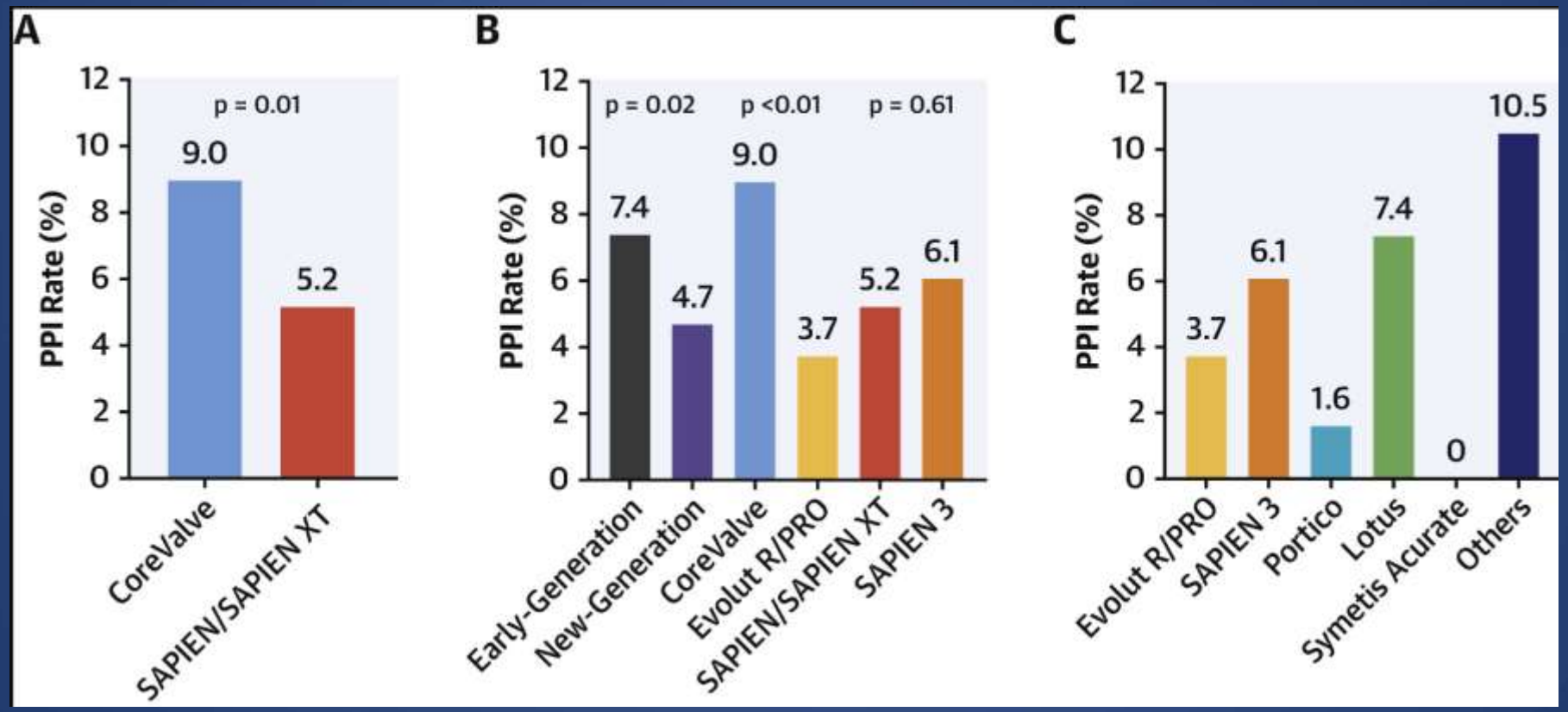
Incidence of valve thrombosis after Mosaic/Hancock VIV = 12.9%

Incidence of valve thrombosis after Mosaic/Hancock VIV and antiplatelet therapy = 20.7% (1 out of every 5 patients)

Danny Dvir, MD. TVT 2017

Permanent pacemaker implantation after Valve-in-valve

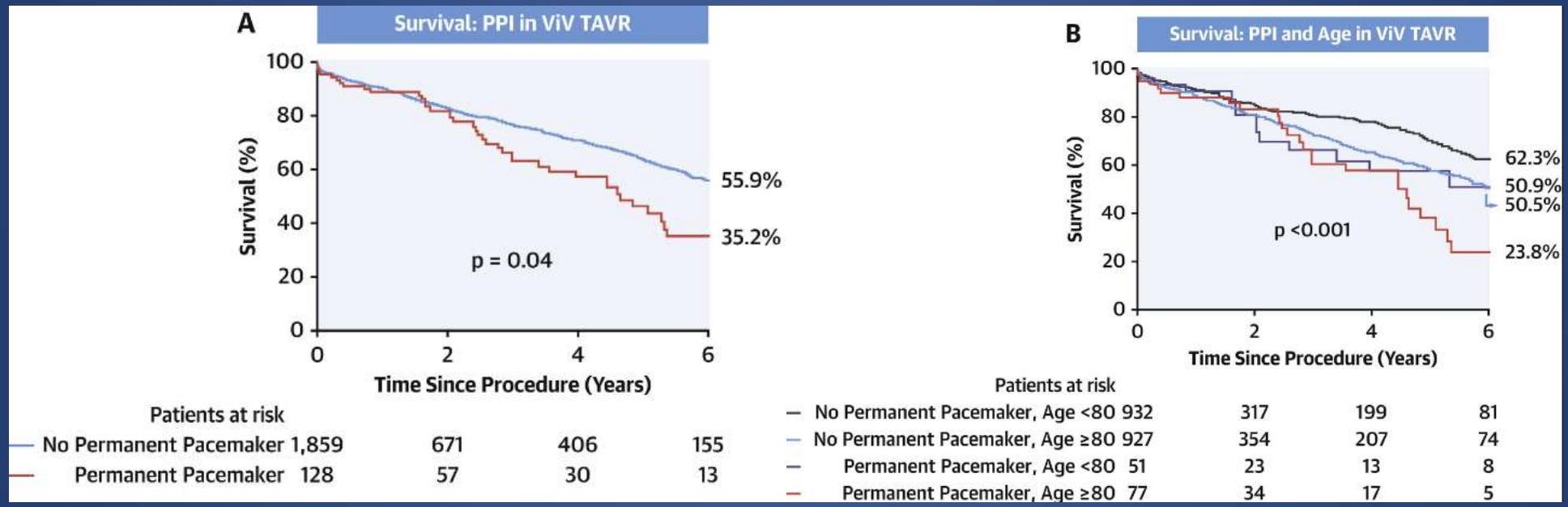
PPI rate after ViV-TAVR for Early- and New-generation Devices



Alperi A, et al., VIVID Registry. J Am Coll Cardiol. 2021 May 11;77(18):2263-2273

Permanent pacemaker implantation after Valve-in-valve

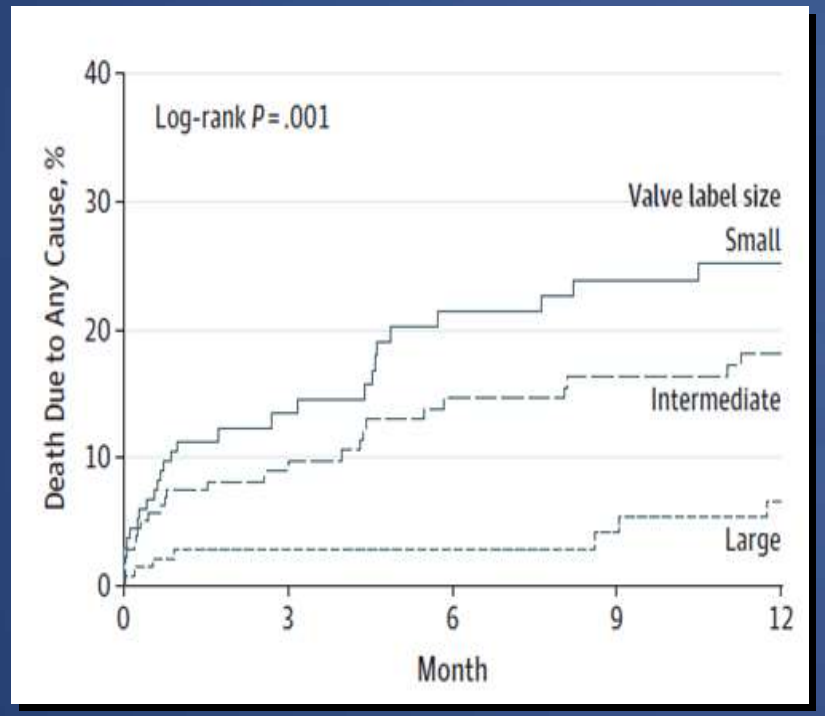
Survival curve After ViV-TAVR by PPI and Age



Alperi A, et al., VIVID Registry. J Am Coll Cardiol. 2021 May 11;77(18):2263-2273

Bioprosthetic Valve Fracture for Optimizing Results of Valve-in-Valve TAVR

Impact of Surgical Valve Size on 1-Year Mortality



VIVID Registry

- 459 pts with failed surgical bioprostheses treated with ViV TAVR (59% balloon expandable, 41% self-expanding)
- Patients stratified based on size of original surgical valve
  - *Small ≤ 21 (n=133)*
  - *Medium 22-24 (n=176)*
  - *Large ≥ 25 (n=139)*
- Small surgical valve independently associated with 1-year mortality (HR 2.04, p=0.02)

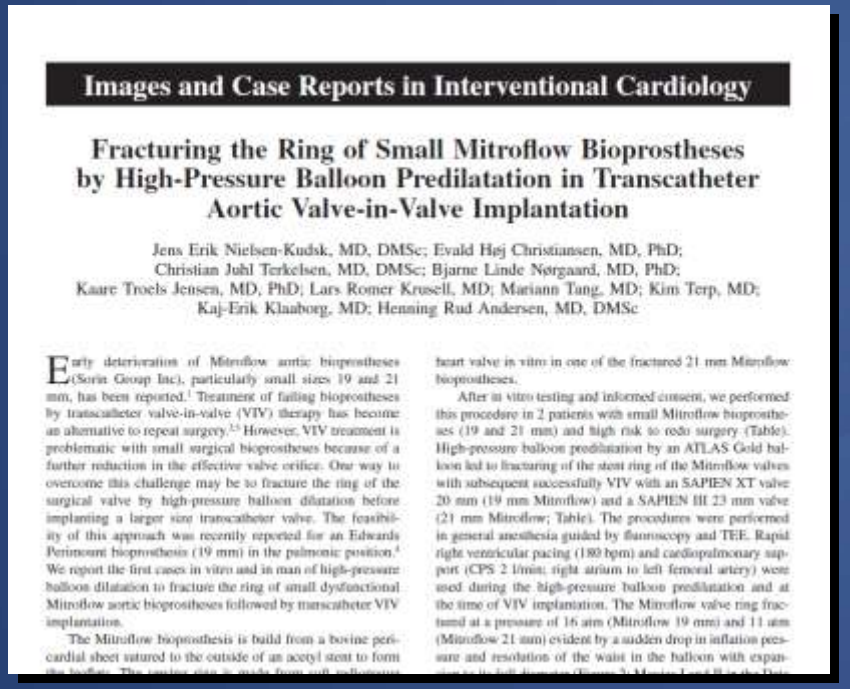
Dvir D, et al. JAMA 2014;312:162-170

Bioprosthetic Valve Fracture in VIV TAVR

- 20 consecutive patients from 7 US centers treated with bioprosthetic valve fracture at the time of ViV TAVR
- Mean age 76 years; mean STS-PROM 8.4%
- Valves treated: Mitroflow, Perimount, Magna/Magna-Ease, Biocor Epic/Epic-Supra, and Mosaic
- Treated with both self-expanding (n=12) and balloon expandable (n=8) TAVR valves
- 15/20 underwent BVF after TAVR valve deployed

Chhatriwalla A, et al. Circ Intv 2017

Fracturing the Ring of small bioprostheses



Images and Case Reports in Interventional Cardiology

Fracturing the Ring of Small Mitroflow Bioprostheses by High-Pressure Balloon Predilatation in Transcatheter Aortic Valve-in-Valve Implantation

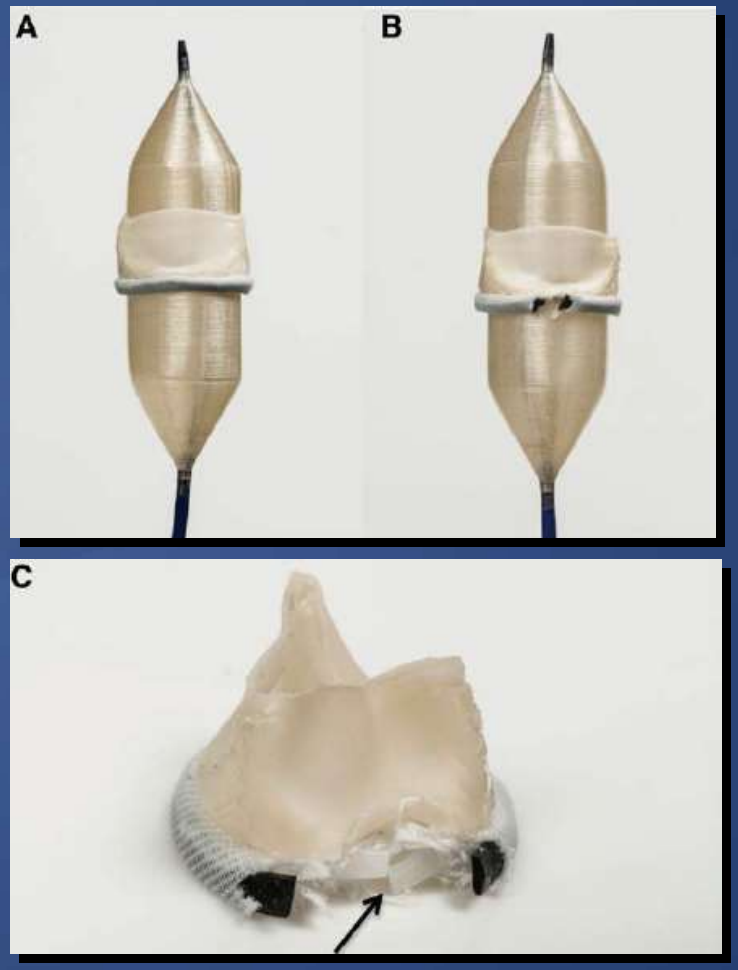
Jens Erik Nielsen-Kudsk, MD, DMSc; Evald Høj Christiansen, MD, PhD; Christian Juhl Terkelsen, MD, DMSc; Bjarne Linde Nørgaard, MD, PhD; Kaare Troels Jensen, MD, PhD; Lars Romer Krusell, MD; Mariann Tang, MD; Kim Terp, MD; Kaj-Erik Klaaborg, MD; Henning Rud Andersen, MD, DMSc

Early deterioration of Mitroflow aortic bioprostheses (Sorin Group Inc), particularly small sizes 19 and 21 mm, has been reported.[1] Treatment of failing bioprostheses by transcatheter valve-in-valve (VIV) therapy has become an alternative to repeat surgery.[2,3] However, VIV treatment is problematic with small surgical bioprostheses because of a further reduction in the effective valve orifice. One way to overcome this challenge may be to fracture the ring of the surgical valve by high-pressure balloon dilatation before implanting a larger size transcatheter valve. The feasibility of this approach was recently reported for an Edwards Perimount bioprosthesis (19 mm) in the pulmonic position.[4] We report the first cases in vitro and in man of high-pressure balloon dilatation to fracture the ring of small dysfunctional Mitroflow aortic bioprostheses followed by transcatheter VIV implantation.

The Mitroflow bioprosthesis is build from a bovine pericardial sheet sutured to the outside of an acetyl stent to form

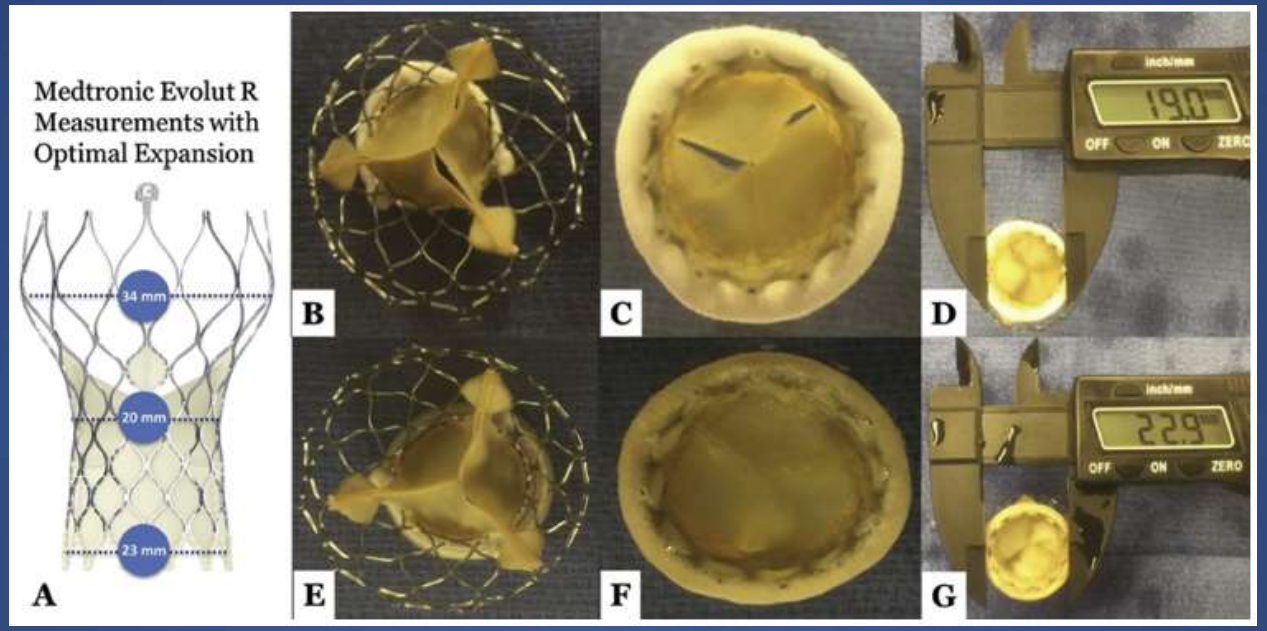
heart valve in vitro in one of the fractured 21 mm Mitroflow bioprostheses.

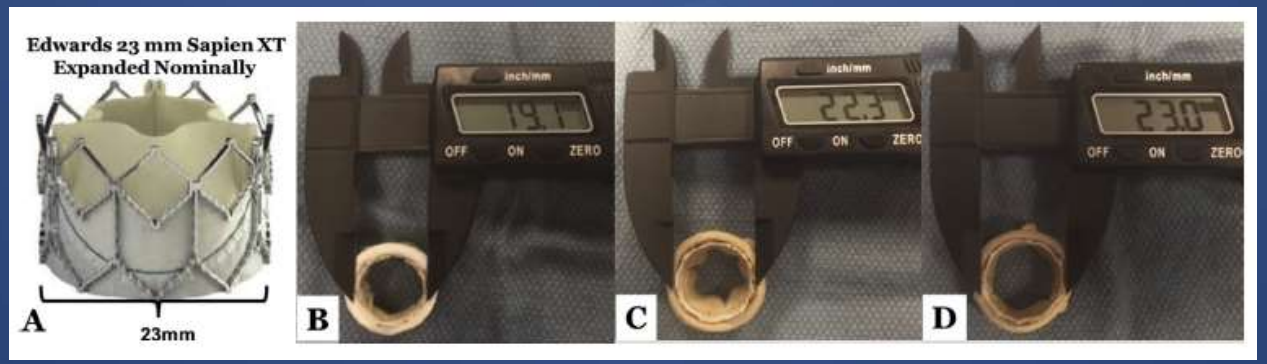
After in vitro testing and informed consent, we performed this procedure in 2 patients with small Mitroflow bioprostheses (19 and 21 mm) and high risk to redo surgery (Table). High-pressure balloon predilatation by an ATLAS Gold balloon led to fracturing of the stent ring of the Mitroflow valves with subsequent successfully VIV with an SAPIEN XT valve 20 mm (19 mm Mitroflow) and a SAPIEN III 23 mm valve (21 mm Mitroflow; Table). The procedures were performed in general anesthesia guided by fluoroscopy and TEE. Rapid right ventricular pacing (180 bpm) and cardiopulmonary support (CPS 2 l/min; right atrium to left femoral artery) were used during the high-pressure balloon predilatation and at the time of VIV implantation. The Mitroflow valve ring fractured at a pressure of 16 atm (Mitroflow 19 mm) and 11 atm (Mitroflow 21 mm) evident by a sudden drop in inflation pressure and resolution of the waist in the balloon with expan-



Nielsen-Kudsk JE, et al. Circ Cardiovasc Intv 2015

Bench Testing





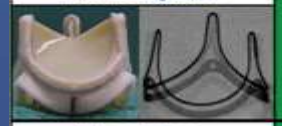
Allen KB, et al. Ann Thorac Surg 2017

Valves that can and cannot be fractured

To date, the only valves that cannot be fractured are:

Trifecta (St. Jude)

Hancock II (MDT)

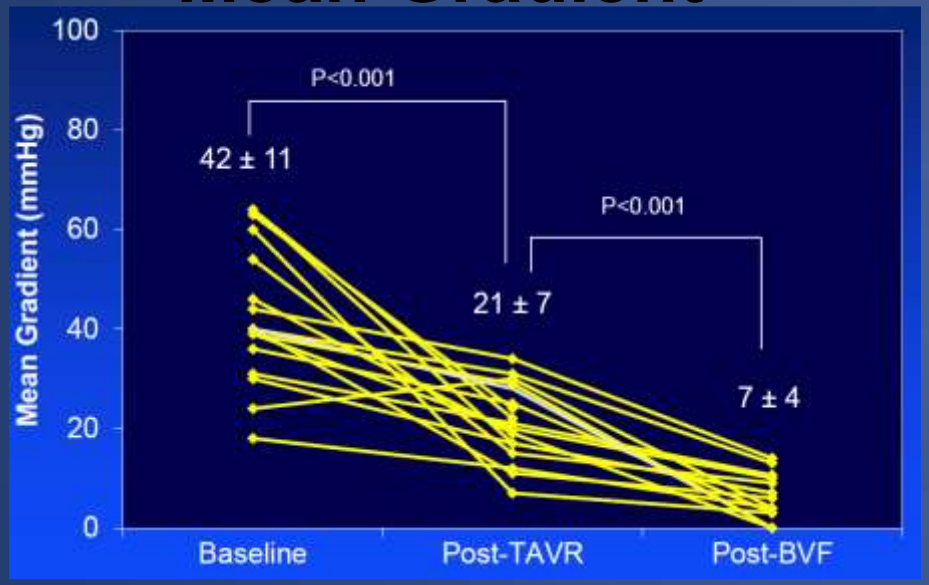
Manufacturer/ Brand	Valve Size	Bard TRU Balloon Fracture/Pressure	Bard Atlas Gold Balloon Fracture/Pressure	Appearance After Fracture
St. Jude Trifecta 	19 mm 21 mm	NO NO	NO NO	
St. Jude Biocor Epic 	21 mm	YES / 8 ATM	YES / 8 ATM	
Medtronic Mosaic 	19 mm 21 mm	YES / 10 ATM YES / 10 ATM	YES / 10 ATM YES / 10 ATM	
Medtronic Hancock II 	21 mm	NO	NO	
Sorin Mitroflow 	19 mm 21 mm	YES / 12 ATM YES / 12 ATM	YES / 12 ATM YES / 12 ATM	
Edwards MagnaEase 	19 mm 21 mm	YES / 18 ATM YES / 18 ATM	YES / 18 ATM YES / 18 ATM	
Edwards Magna 	19 mm 21 mm	YES / 24 ATM YES / 24 ATM	YES / 24 ATM YES / 24 ATM	

1. Balloons sized 1 mm larger than valve size.
2. Medtronic Mosaic and Sorin Mitroflow have no metal in ring therefore appearance after fracture unchanged.

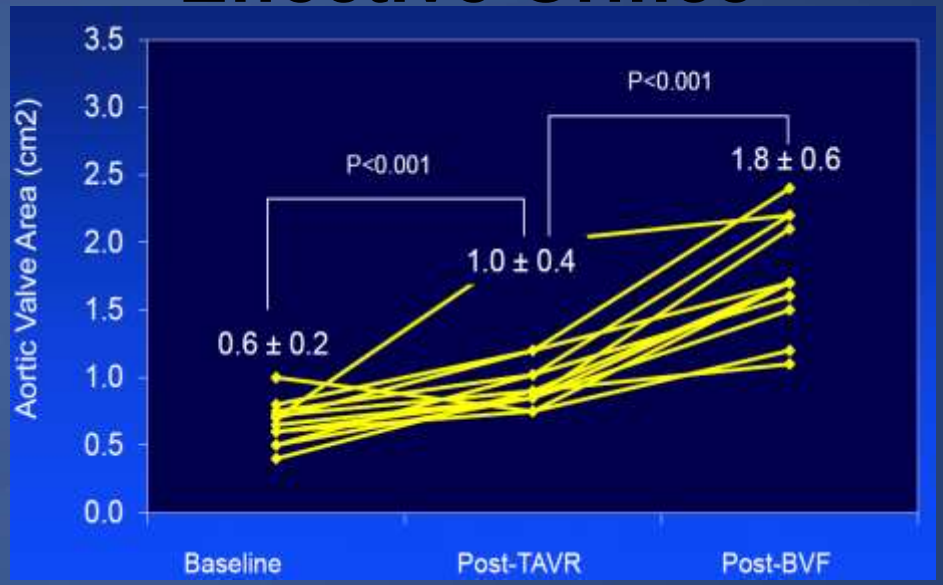
Allen KB et al. Ann Thorac Surg 2017

Bioprosthetic Valve Fracture in VIV TAVR

Mean Gradient



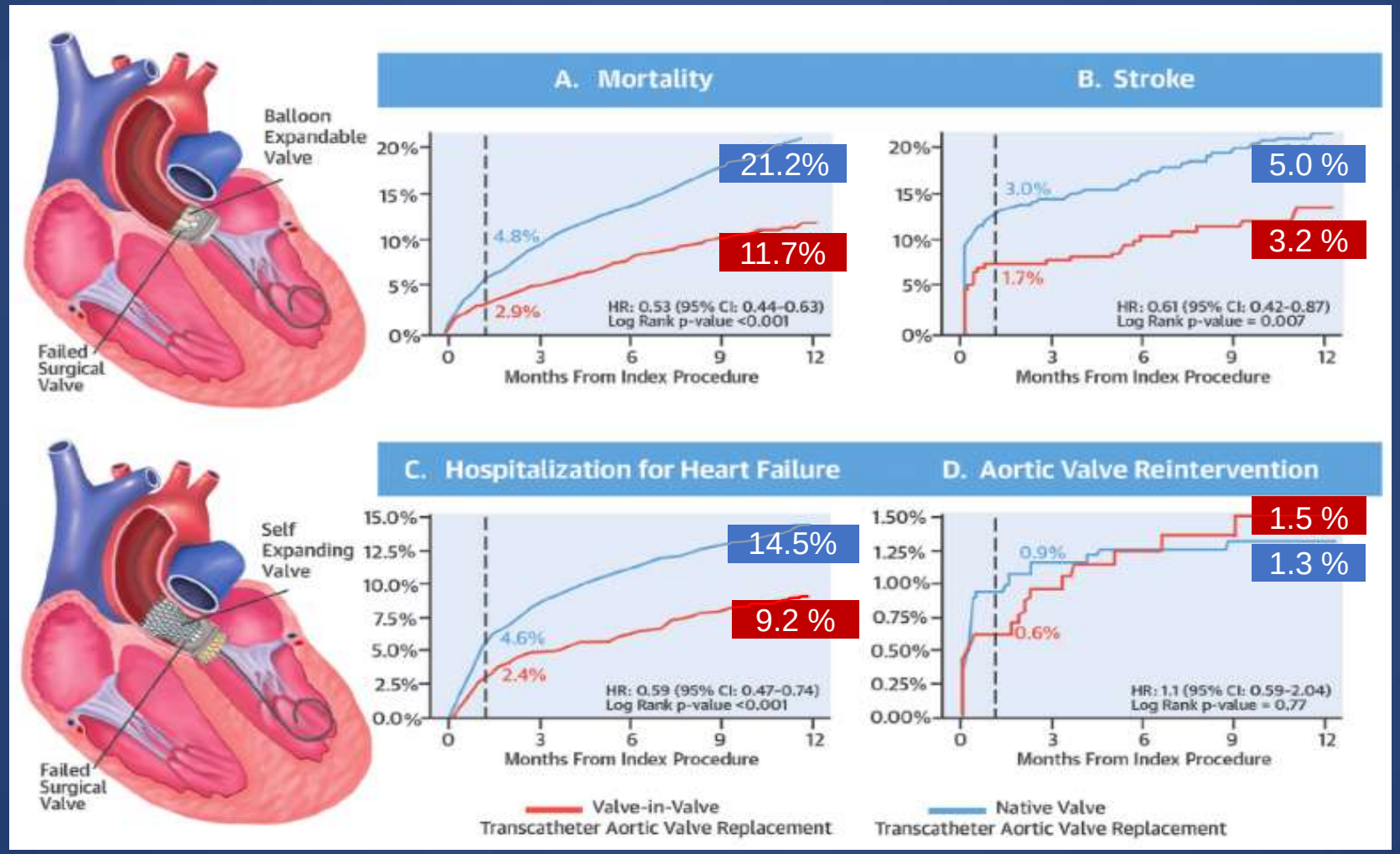
Effective Orifice



To date, BVF can be performed safely in small surgical valves. However, the safety of this technique is not fully evaluated. Unresolved questions : Timing of BVF (pre vs. post-TAVR)

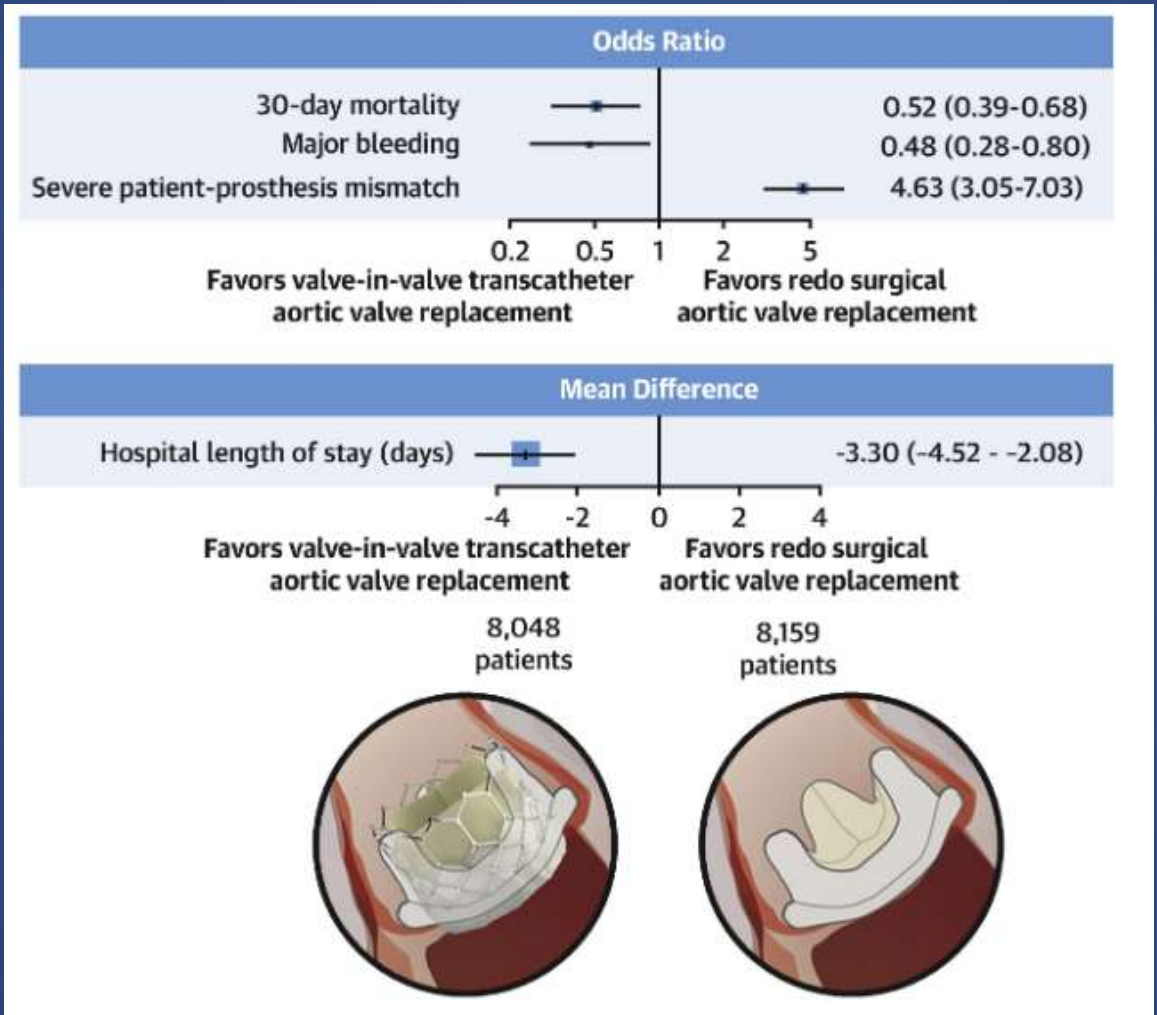
David J. Cohen, MD. TVT 2017
Chhatriwalla A, et al. Circ Intv 2017

ViV TAVR Versus TAVR for Native Aortic stenosis



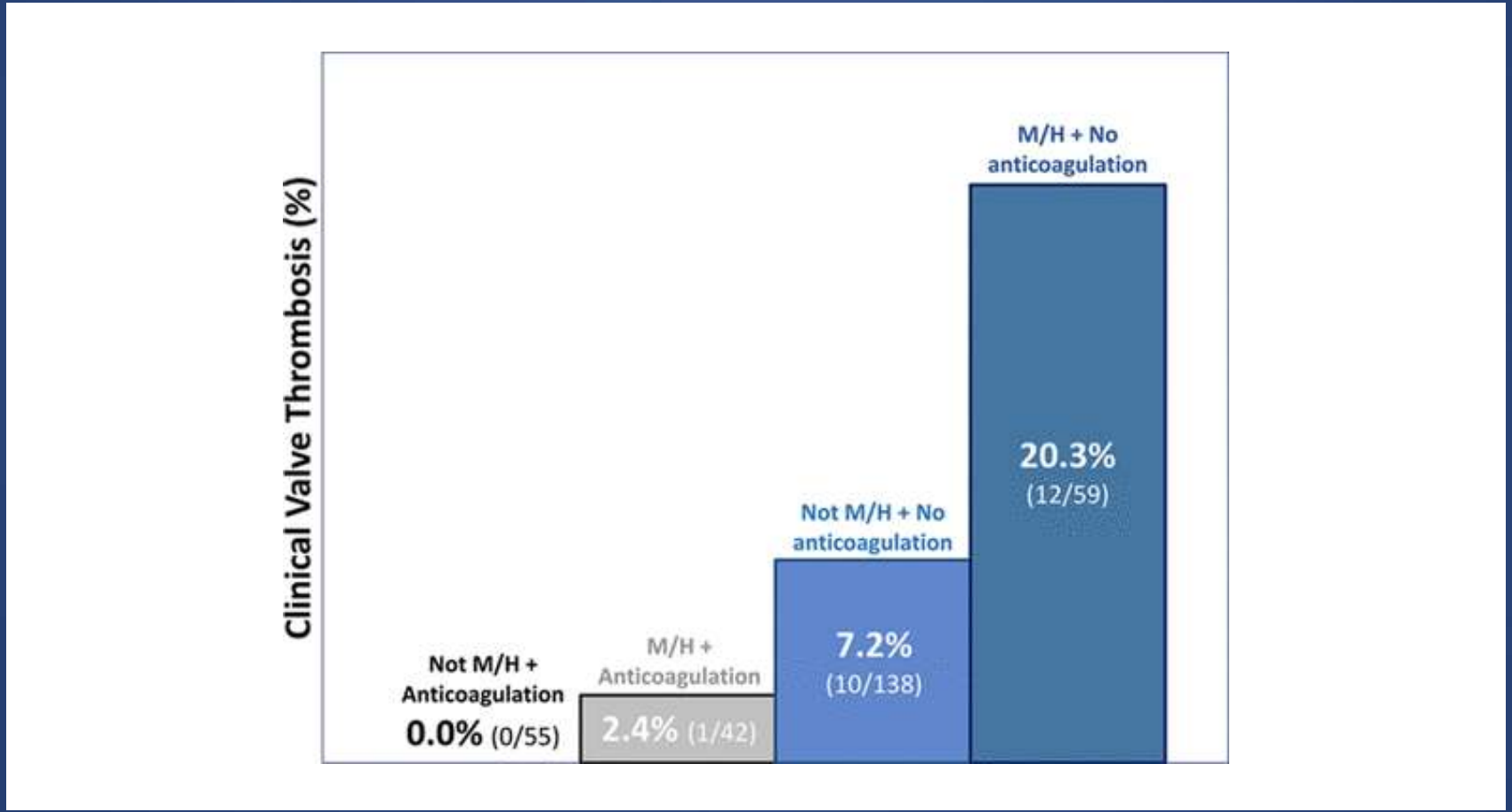
Tuzcu, E.M. et al. JACC 2018

ViV TAVR Versus redo-SAVR for Bioprosthetic aortic valve dysfunction



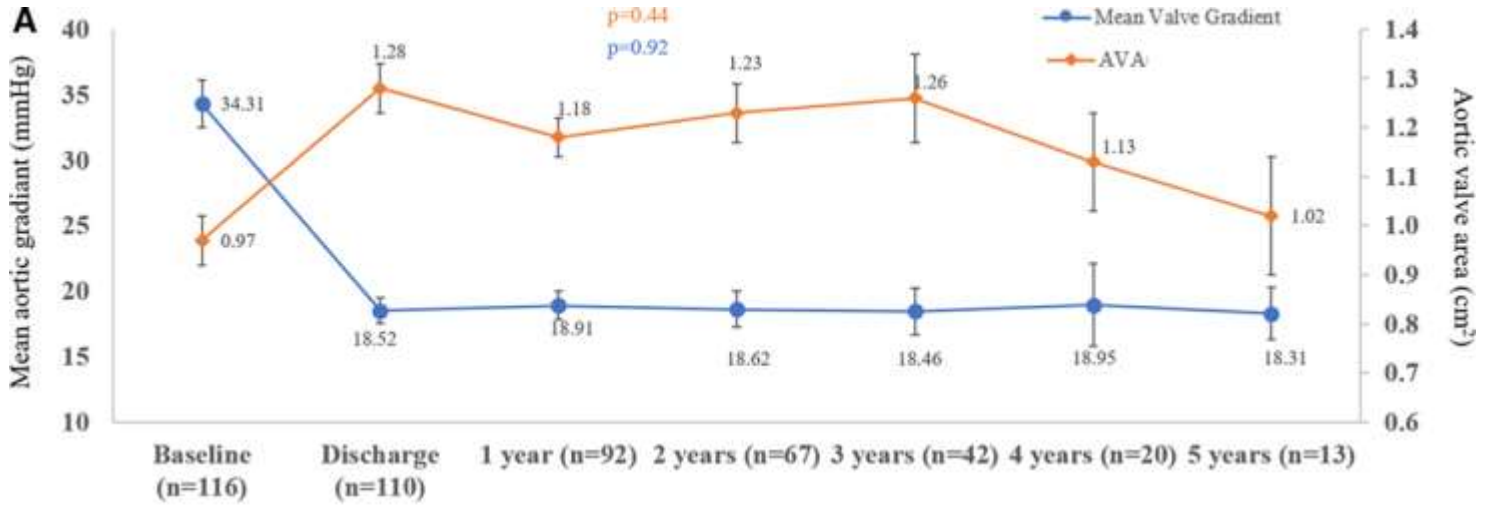
Sa, M.P.B.O. et al. JACC Intv. 2021;14(2):211-20

Clinical Valve Thrombosis after Transcatheter Aortic ViV Implantation



Mohamed Abdel-Wahab et al, CIRC intv 2018

Long-Term Outcomes After Transcatheter Aortic ViV Replacement



Leonard de Freitas Campos Guimaraes et al, CIRCINTERVENTIONS, 2018

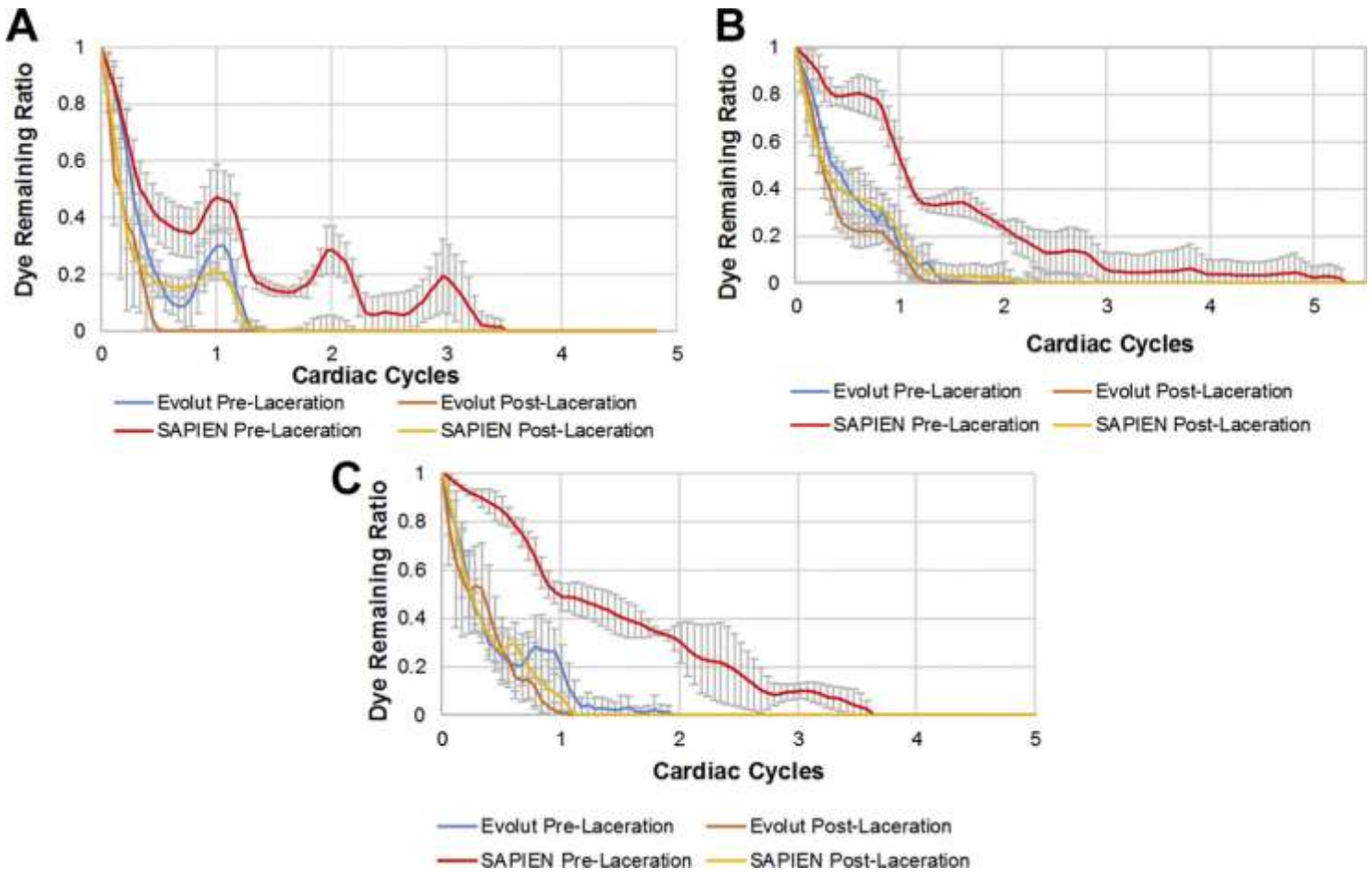
ViV TABR for Degenerated SBAV : Multicenter Retrospective Analysis

- **Among 66 SBAV, Mortality 3.0% at 30 days and 9.6% at 1 year.**
- **At 1 year, LVED was decreased versus baseline : 3.0 [2.6 to 3.6] cm vs. 3.7 [3.2 to 4.4] cm ($p < 0.001$)**
- **Coronary occlusion (9.1%) resulted in myocardial infarction (3.0%).**
- **Predictors of coronary occlusion**
  Subcoronary implant technique compared with full root replacement
  Short simulated radial valve-to-coronary distance
  Low coronary height

Conclusions: TAVR in SBAVs is frequently associated with high-risk coronary anatomy but can be performed with a low risk of death and myocardial infarction, resulting in favorable ventricular remodeling. A subcoronary surgical approach is associated with an increased risk of coronary obstruction.

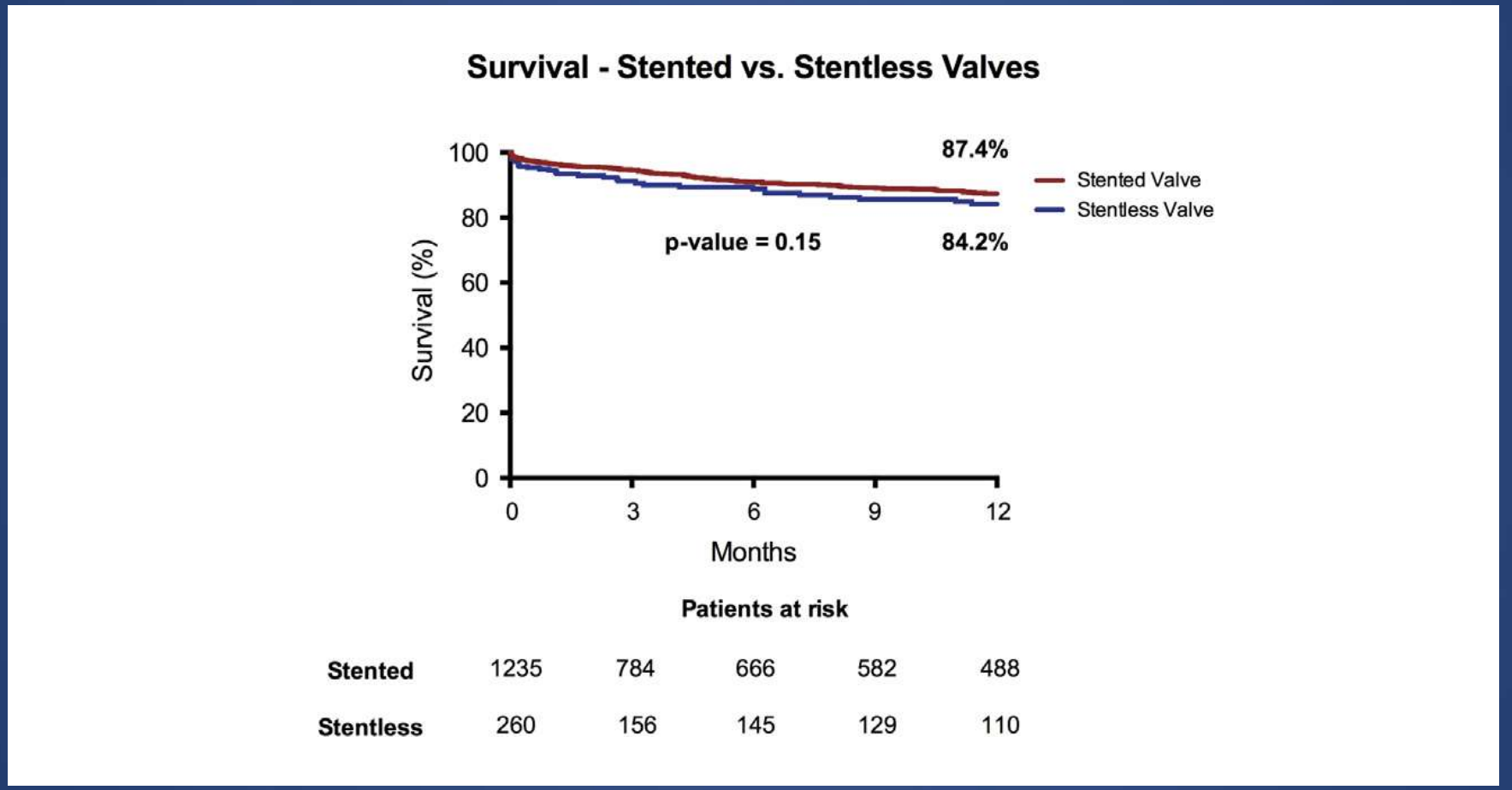
Miller M, et al. JACC Intv 2019

Impact of Leaflet Laceration on Transcatheter Aortic ViV Washout



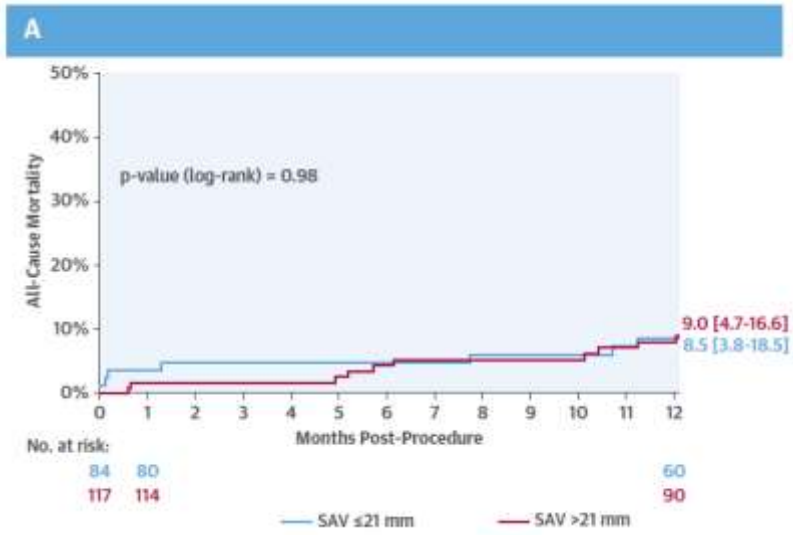
Hoda Hatoum et al, JACC intv 2019

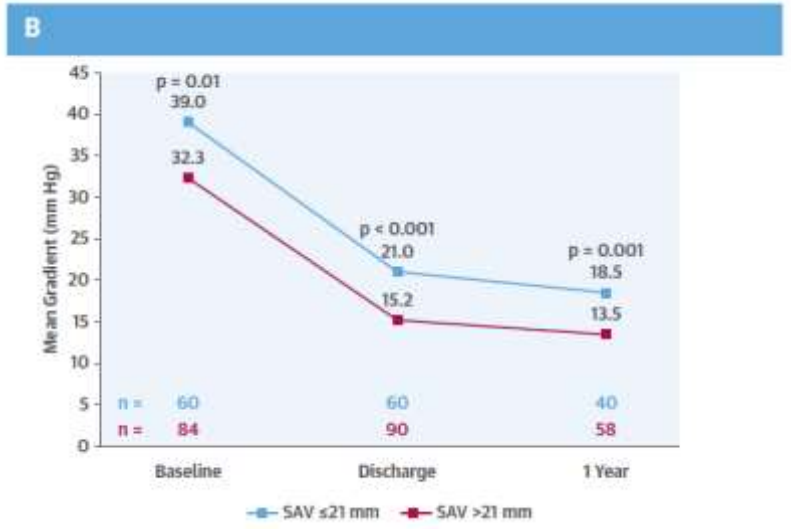
ViV-TAVR
Stentless vs stented Valves



Duncan et al., JACC intv 2019

Clinical and Echocardiographic Outcomes According to Surgical Valve Size

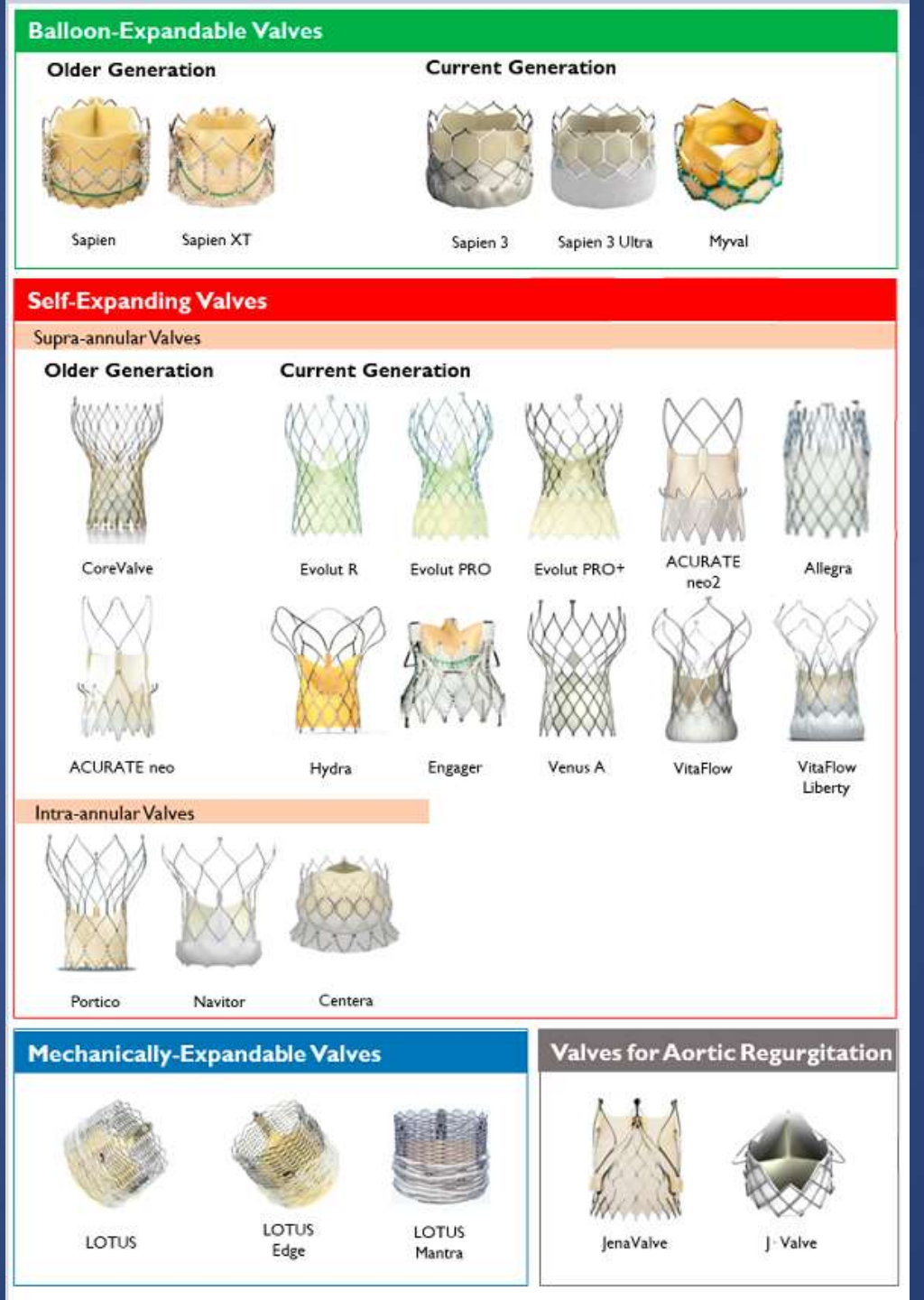




Tchétché, D. et al., JACC Intv 2019

New TAVR Devices

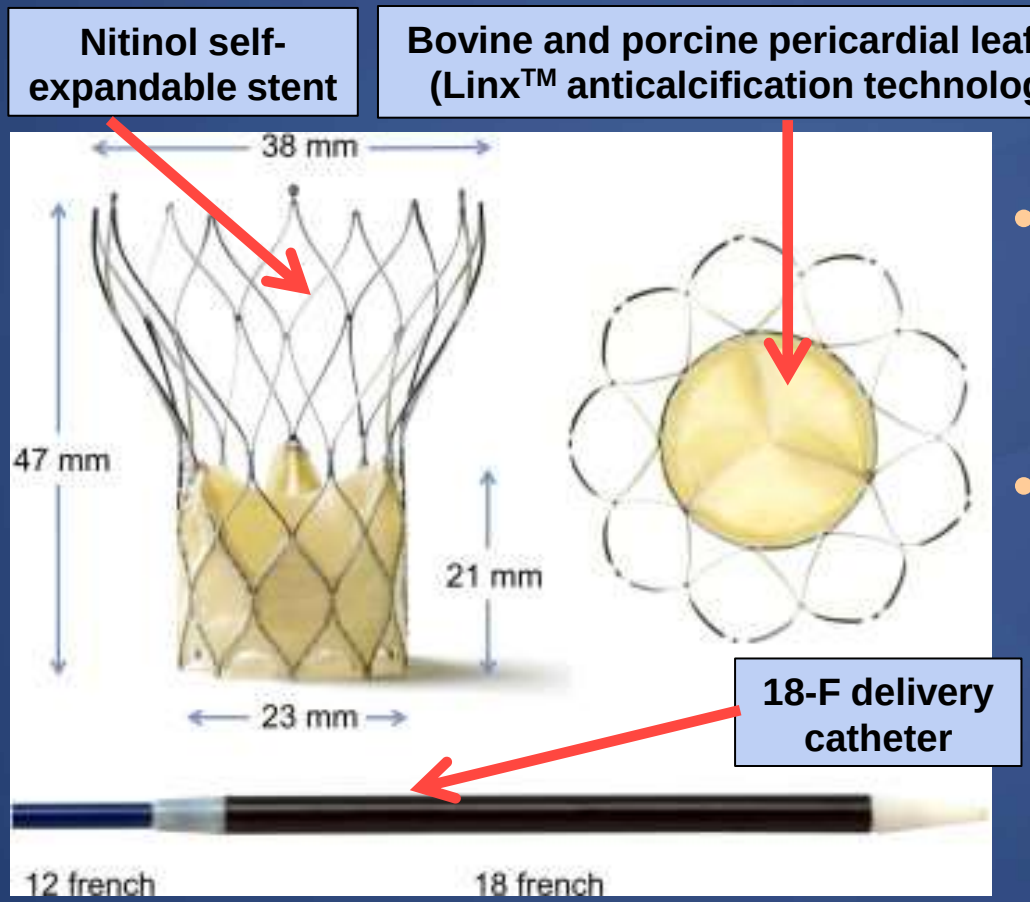
Older & Current



Mauro Chiarito et al. *J. Clin. Med.* 2022, *11*(15)

St. Jude Medical Portico Valve

Next Generation Design Features



- Open stent cell allows access to coronaries and low crimp profile
- Low placement of leaflets/cuff within stent frame allows for minimal protrusion into the LVOT

TAVR with St. Jude Medical Portico Valve: First-in-Human Experience

New valve with repositionable features implanted in 10 pts with severe AS

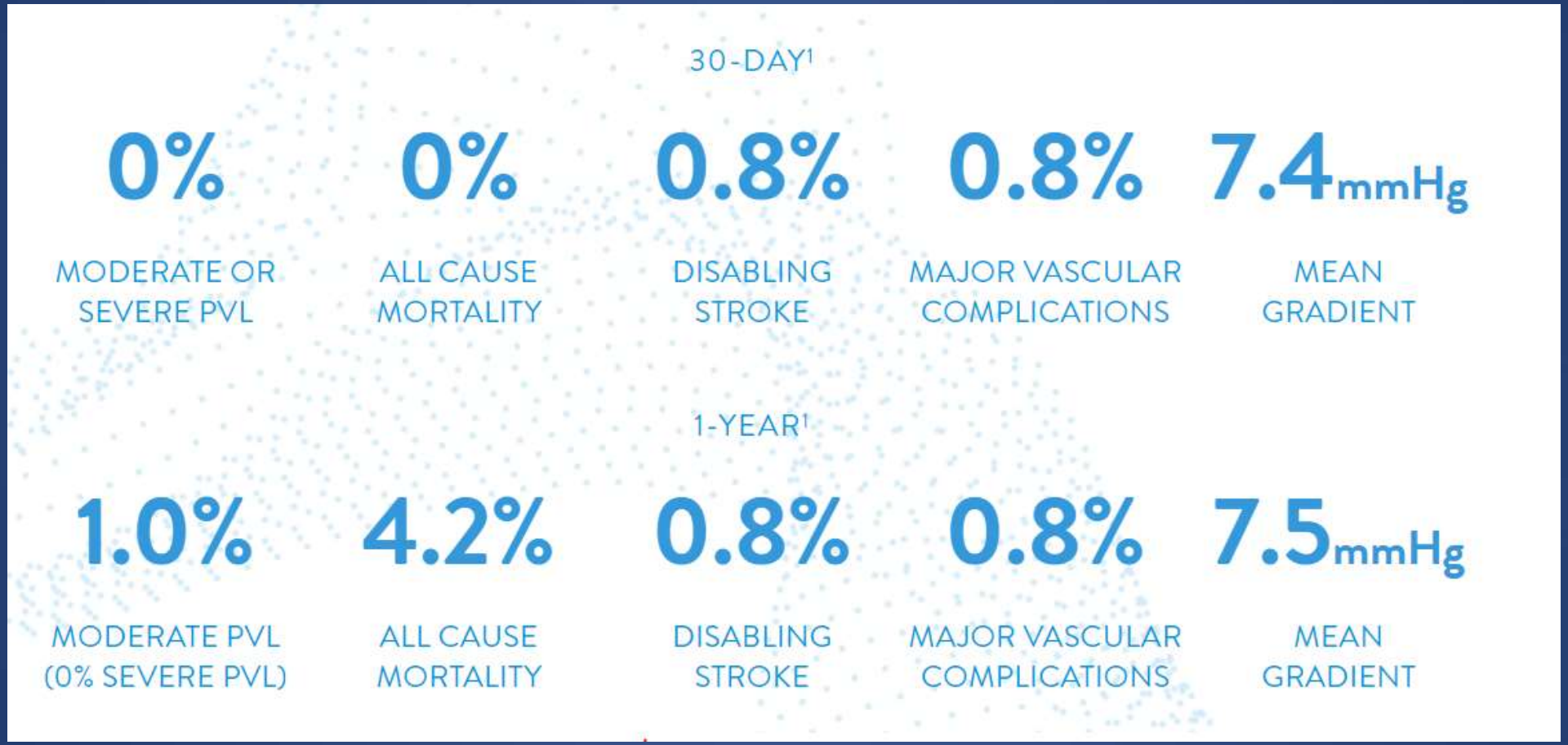
- Device implantation was successful in all pts; valve recapture/repositioning performed in 4 cases
- At 30 days, no major strokes, major vascular complications, major bleeds, or deaths
- Mean transaortic gradient on echo reduced from 44.9 mm Hg to 10.9 mm Hg ($P < 0.001$)

J Am Coll Cardiol. 2012 Aug 14;60(7):581-6. Epub 2012 May 30

Navitor™

- Smart sealing mitigates PVL
- Uncompromised coronary access
- 14F delivery system with 5.0 mm minimum vessel diameter
- Recapturable, repositionable, and retrievable design

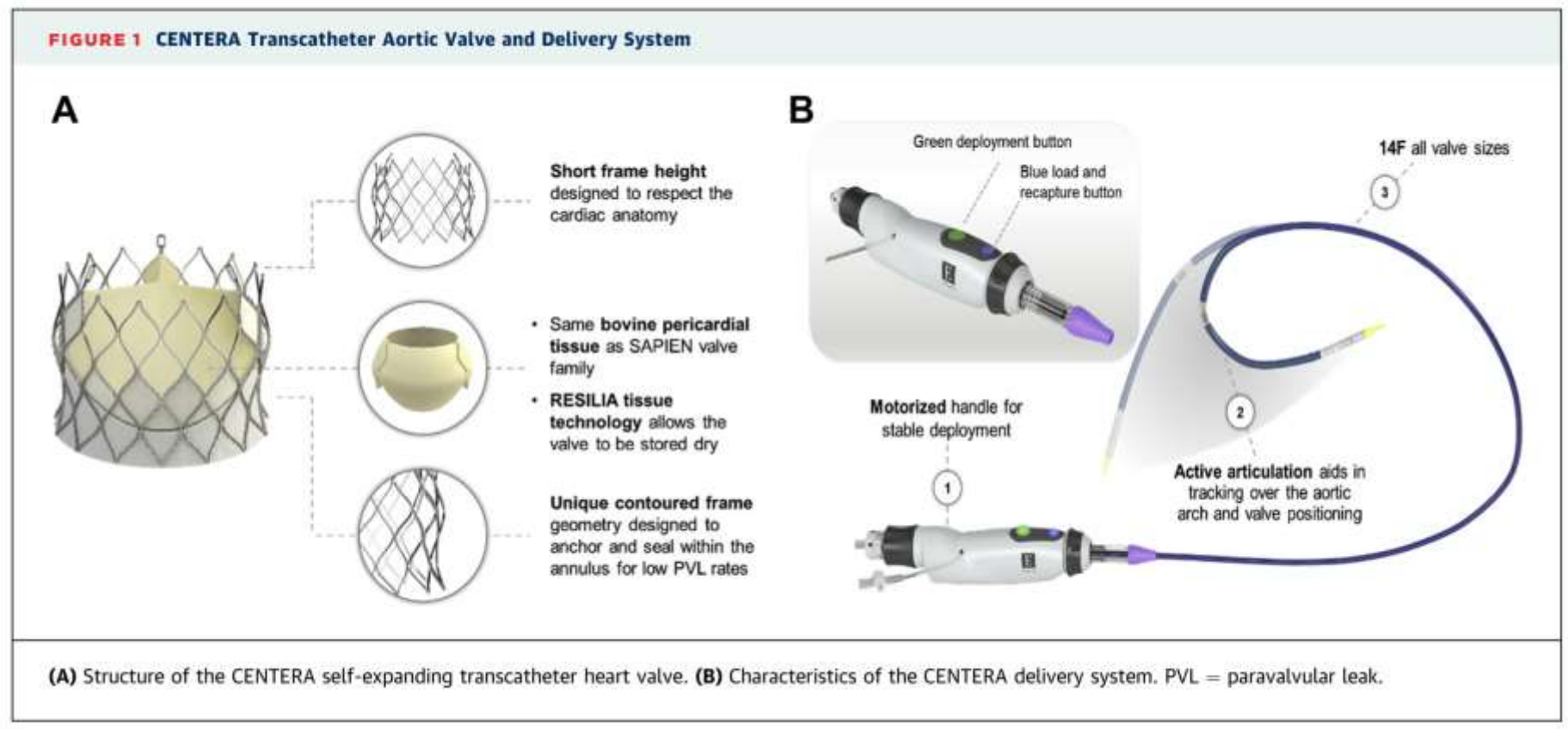
Navitor™



1.Smith, D. One-year clinical trial results with a next-generation aortic transcatheter heart valve. Presented at: EuroPCR conference; May 17-20, 2022.
2.Forrest JK, Mangi AA, Popma JJ, et al. Early outcomes with the Evolut PRO repositionable self-expanding transcatheter aortic valve with pericardial wrap. *J Am Coll Cardiol Intv.* 2018;11:160-168.
3.Möllmann H, Holzhey DM, Hilker M, et al. The ACURATE neo2 valve system for transcatheter aortic valve implantation: 30-day and 1-year outcomes. *Clin Res Cardiol.* 2021 Dec;110(12):1912-1920.
4.Webb J, Gerosa G, Lefèvre T, et al. Multicenter evaluation of a next-generation balloon-expandable transcatheter aortic valve. *J Am Coll Cardiol.* 2014;64:2235-43.
5.Wyler von Ballmoos MC, Reardon MJ, Williams MR, et al. Three-Year Outcomes With a Contemporary Self-Expanding Transcatheter Valve From the Evolut PRO US Clinical Study. *Cardiovasc Revasc Med.* 2021 May;26:12-16.
6.Webb, J. 1-year outcomes from the Sapien 3 Trial. Presented at: EuroPCR conference; May 19-22, 2015.

CENTERA

A low-profile self-expanding nitinol Edward valve



Didier Tchetche et al. JACC intv 2019;12:673-80.

CENTERA

1 year outcomes from CENTER-EU trial

TABLE 2 Clinical Outcomes at 30 Days and 1 Year in the As-Treated Population (CEC Adjudicated)

Safety Endpoints	Kaplan-Meier (n = 203)	
	30 Days	1 Year
All-cause mortality	1.0 (2)	9.1 (18)
Cardiovascular mortality	1.0 (2)	4.6 (9)
Stroke	4.0 (8)	7.6 (15)
Disabling stroke	2.5 (5)	4.1 (8)
Nondisabling stroke	1.5 (3)	4.1 (8)
Myocardial infarction	1.5 (3)	2.0 (4)
New onset atrial fibrillation	8.0 (16)	11.6 (23)
Cardiac-related rehospitalization	0.5 (1)	6.8 (13)
New conduction abnormalities	24.7 (50)	29.4 (59)
Overall PPMI (as treated)	4.9 (10)	6.0 (12)
Naive PPMI (n = 187)	5.4 (10)	6.5 (12)
Life-threatening or disabling bleedings	4.9 (10)	NA*
Major bleedings	14.4 (29)	NA*
Valve prosthesis endocarditis	0 (0)	0.5 (1)
Structural valve deterioration requiring reintervention	0 (0)	0 (0)

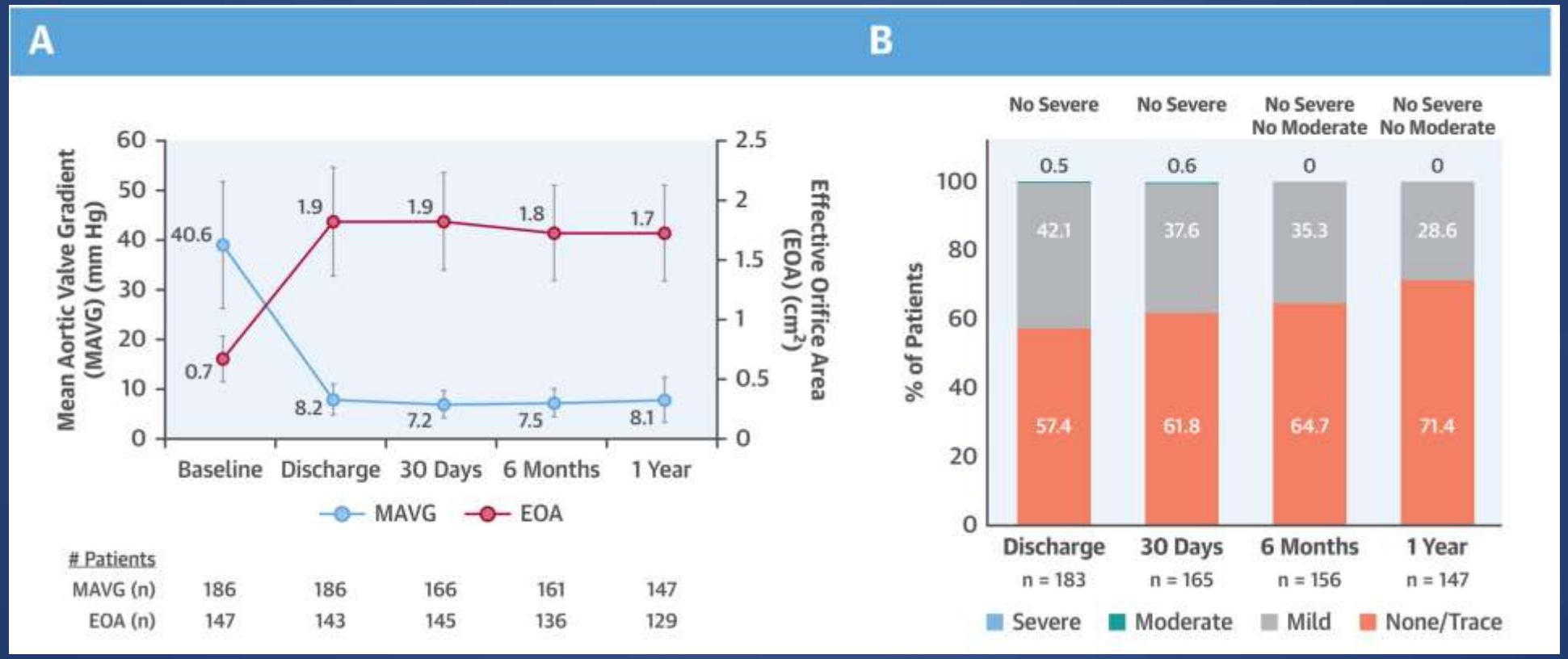
Values are % (n). *Bleedings were adjudicated up to 30 days only.

CEC = Clinical Events Committee; NA = not applicable; PPMI = permanent pacemaker implantation.

Didier Tchetche et al. JACC intv 2019;12:673-80.

CENTERA

1 year outcomes from CENTER-EU trial



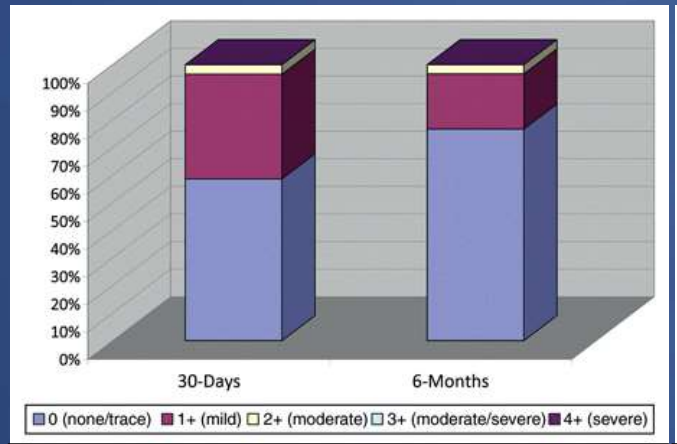
Didier Tchetche et al. JACC intv 2019;12:673-80.

Symetis Acurate TA™ Aortic Bioprosthesis

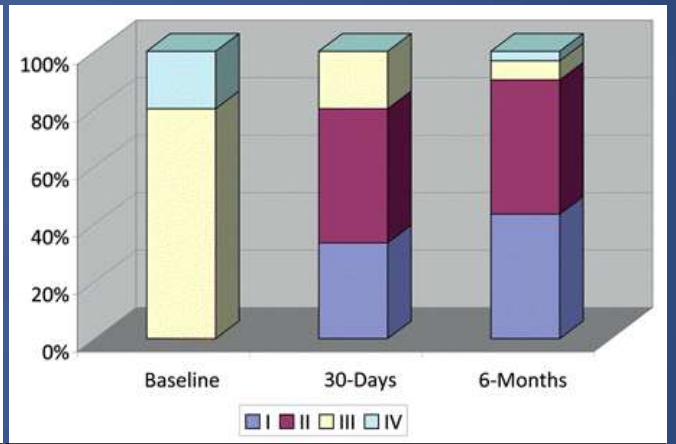
- Porcine pericardium
- Self-expanding nitinol stent
- Stent covered inside and out with double porcine pericardium skirt

ACURATE™ Highlights

- **Trans Apical**
  - FIM (n=40) 6mo. results (EACTS 2011)
    - stable valve function with low rates of paravalvular leakages.
    - good clinical outcomes and 6-month survival



Paravalvular leak over (Echo)



Clinical status (NYHA class) over time

Eur J Cardiothorac Surg. 2012 Apr 4. [Epub ahead of print]

ACURATE™ Highlights

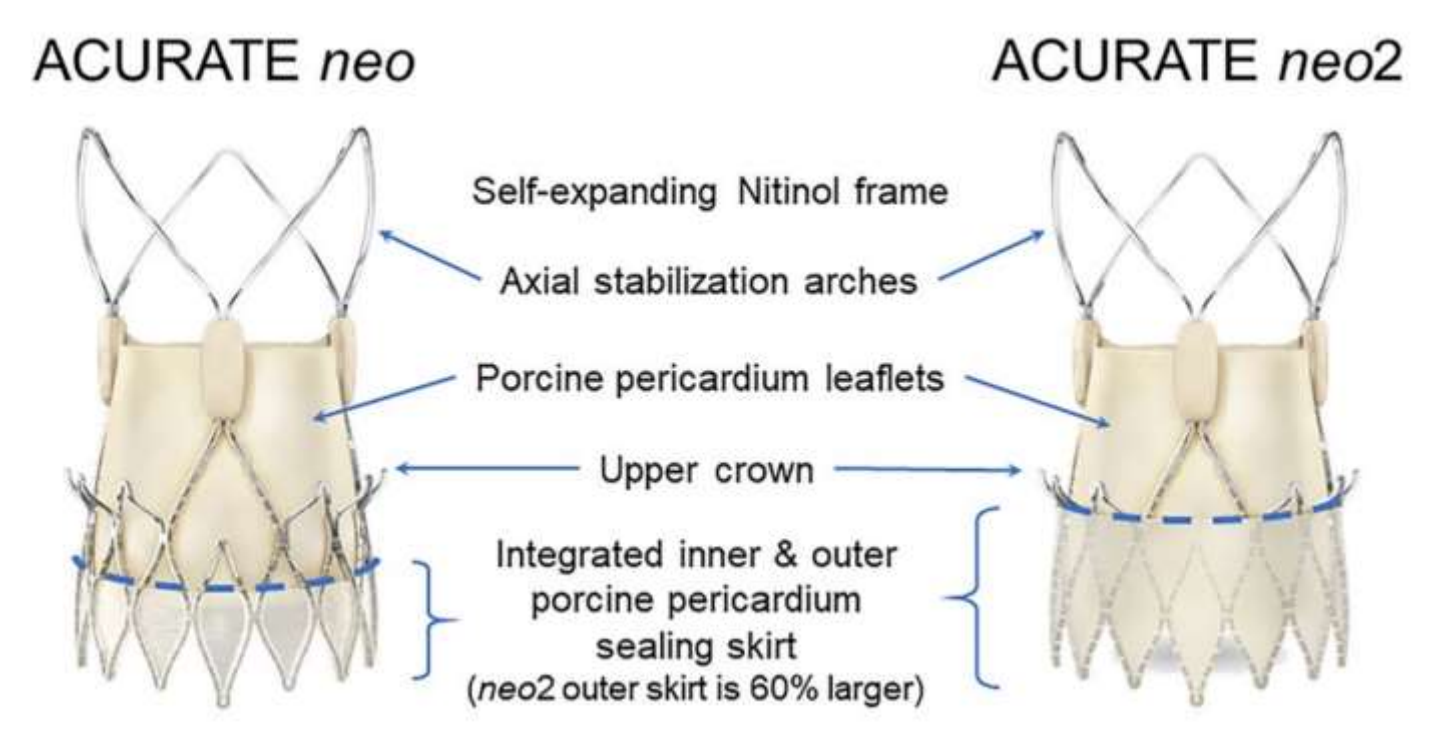
- **Trans Apical**
  - Pilot (n=50) 30days results (TCT 2011)
  - FIM (n=40) 1Y results (AHA 2011)
  - Pivotal (n=150) enrollment start, 2011(4th quarter)
  - SAVI post-market registry (n=250) with commercial implants

  * Received CE Certification in November 2011 for commercial use

- **Trans Femoral**
  - FIM (n=20) enrollment start, 2012(1st quarter) (Brazil/Germany/France)
  - Pilot (n=50) enrollment start, 2012(3rd quarter)

Eur J Cardiothorac Surg. 2012 Apr 4. [Epub ahead of print]
Methodist Debakey Cardiovasc J. 2012 Apr;8(2):9-12

ACURATE neo2



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Methodist Debakey Cardiovasc J. 2012 Apr;8(2):9-12

ACURATE neo2

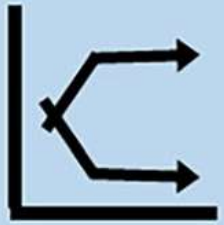
ACURATE *neo2* demonstrates sustained safety and performance for TAVI

Favorable clinical outcomes

All-cause mortality
- **3.3%** @30d
- **11.9%** @12m

Disabling stroke
- **1.7%** @30d
- **No new strokes** @12m

Significantly improved hemodynamics



Mean Pressure Gradient

38.9 mmHg @baseline → **7.8 mmHg** @12m

Effective Orifice Area

0.8 cm² @baseline → **1.7 cm²** @12m

Minimal paravalvular leak

PVL @12m

97.5% ≤ mild

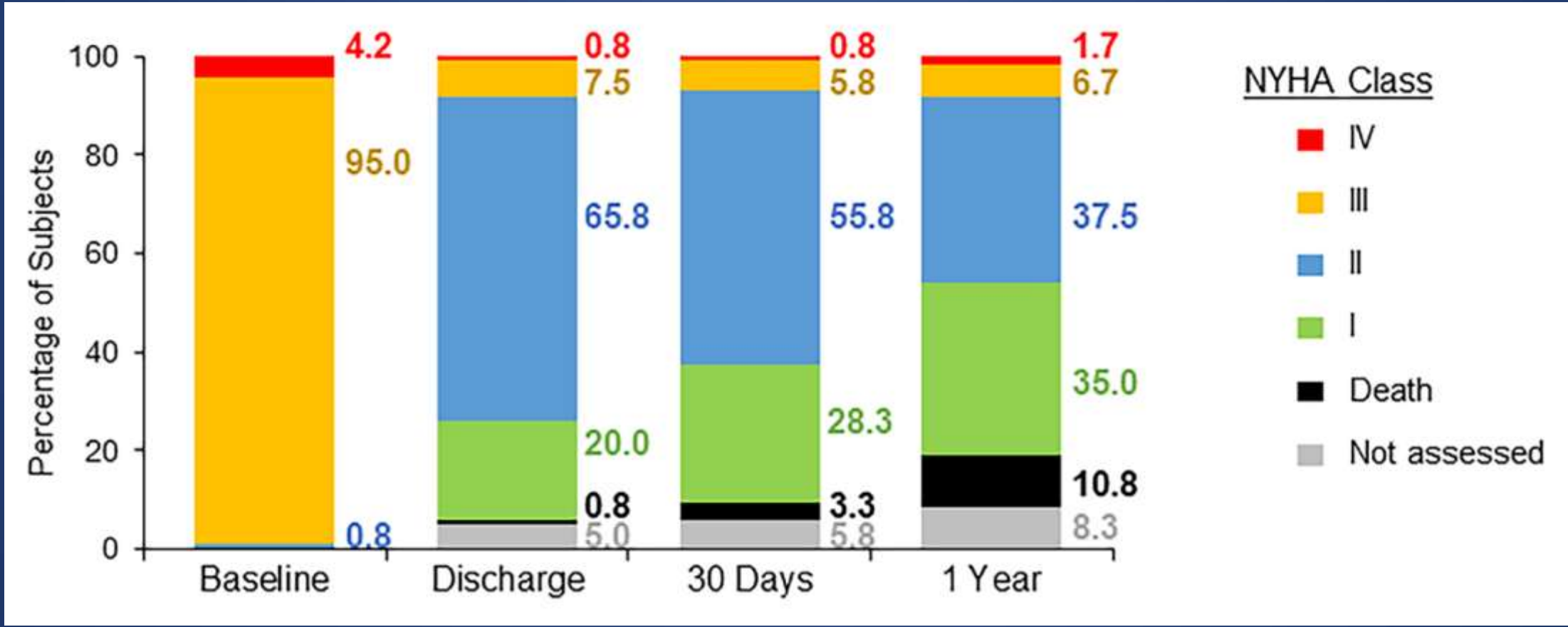
2.5% moderate

0% severe

Clinical Research in Cardiology (2021) 110:1912–1920

ACURATE neo2

Both mean aortic valve gradient and men effective orifice area improved(p<0.001)
Inter-individual improvement in paravalvular leak



Clinical Research in Cardiology (2021) 110:1912–1920

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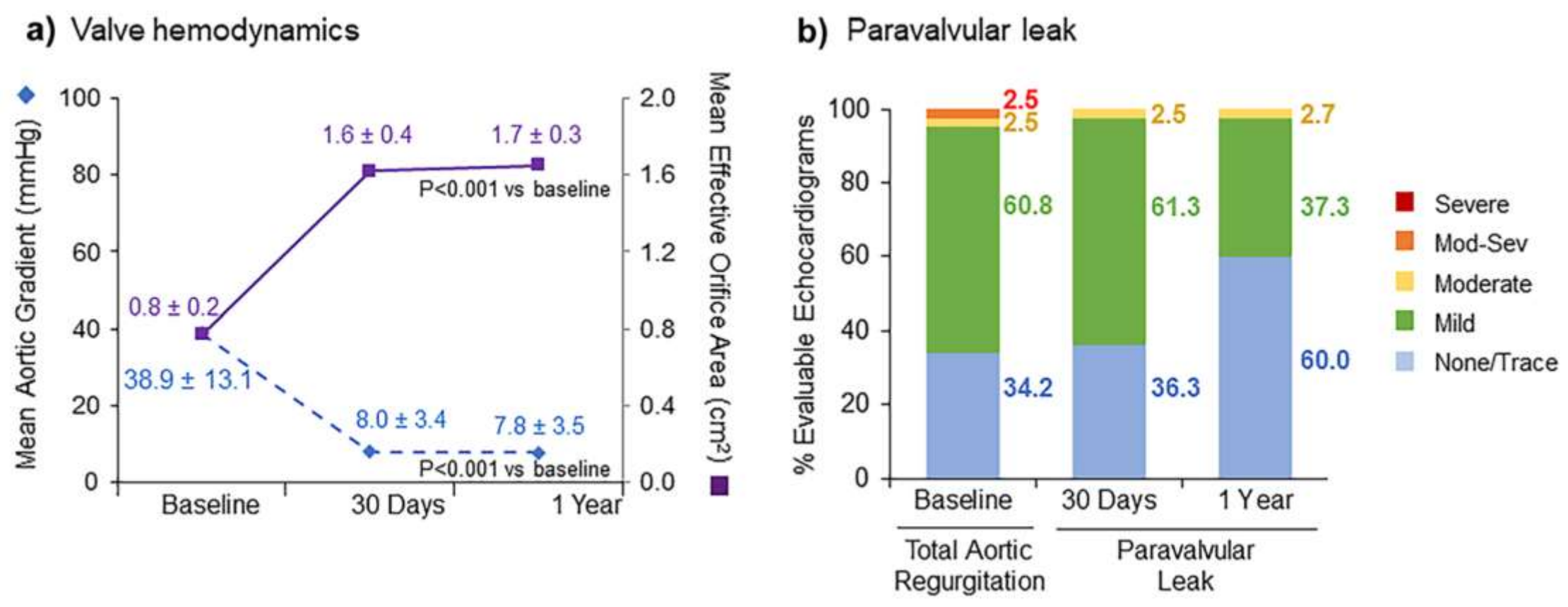


Clinical Research in Cardiology (2021) 110:1912–1920

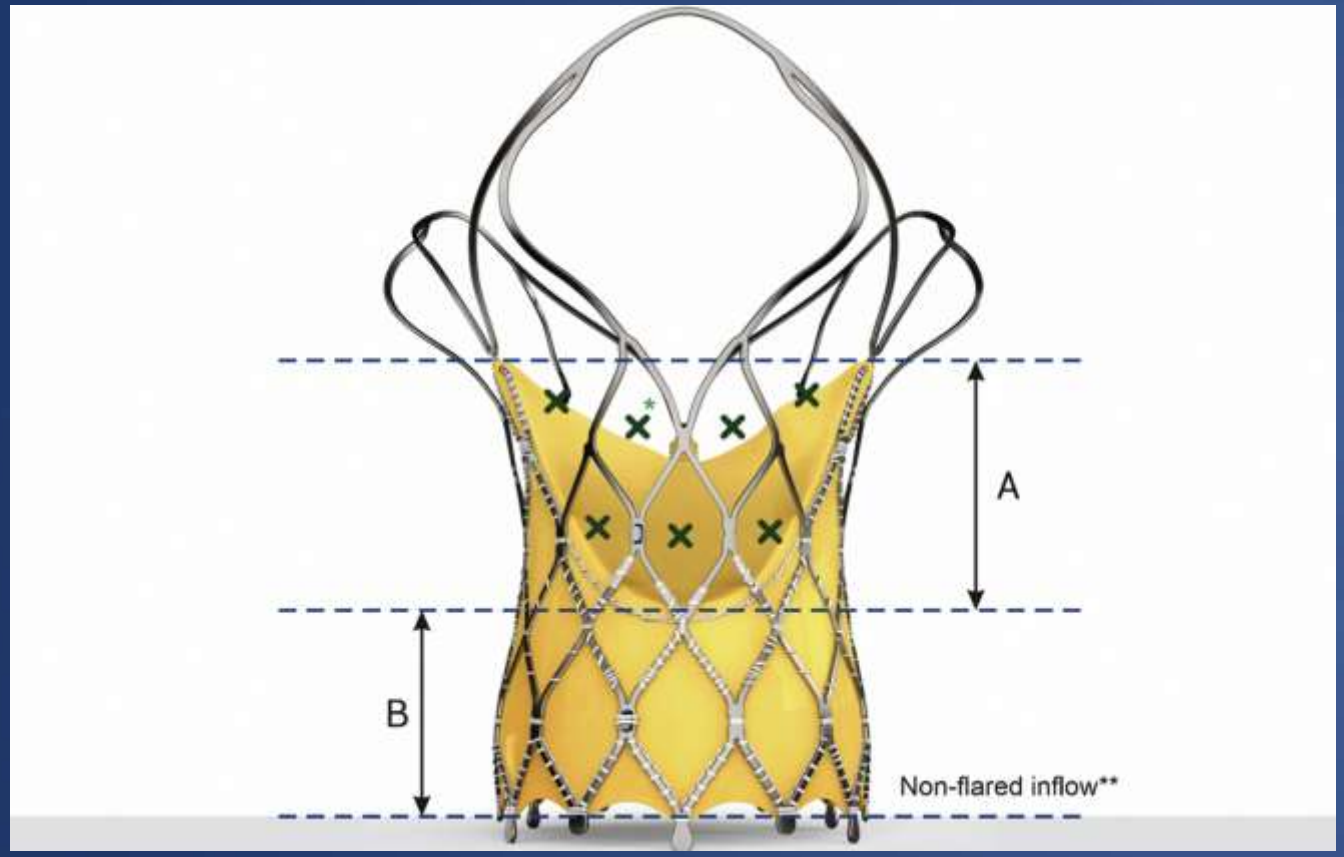
ALLEGRA

Durability
- Bovine pericardium, selected in material thickness and elasticity
- Robust, self-expanding, lasered nitinol stent
- Leaflet stress reduction through flexible commissural fixation points

Control
- T-Bars facilitate safe anchoring to the catheter
- Radiopaque marker rings for accurate positioning
- Sqeeze-to-Release mechanism allows for stepwise and controlled implantation

Flow
- 12 mm sealing area minimized the risk of paravalvular leakage

Hydra



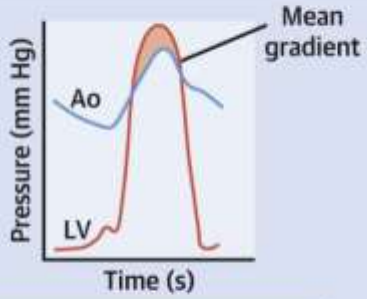
- 3 Bovine pericardium leaflet
- Self-expandable nitinol stent frame
- X - Large cells facilitates easy access to the coronary arteries and flexibility of the delivery catheter
- A – Supra-annular position of leaflets provides large effective orifice area and low trans-valvular gradient
- B – High sealing skirt mitigates paravalvular leak

Aidietis, A.et al. J Am Coll Cardiol Intv. 200;15(1):93-104.

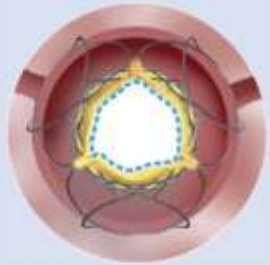
Hydra

CENTRAL ILLUSTRATION: Safety and Clinical Performance of Hydra Self-Expanding Transcatheter Aortic Valve

Hydra Transcatheter Heart Valve Offered Favorable Efficacy as Well as Low Complication Rates: Hydra CE Study

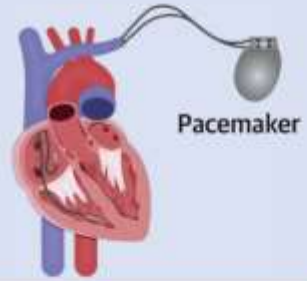


Mean aortic valve gradient at 30 days: 8.1 mm Hg



Mean effective orifice area at 30 days: 1.9 cm^2

Hydra Transcatheter Heart Valve



New permanent pacemaker at 30 days: 11.7%

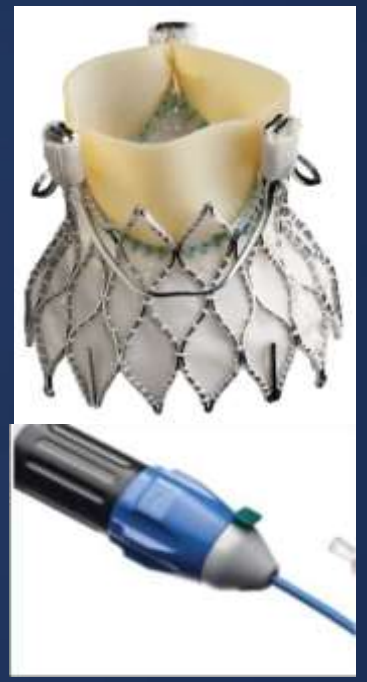
≥ Moderate paravalvular leak at 30 days: 6.3%

Aidietis, A.et al. J Am Coll Cardiol Intv. 200;15(1):93-104.

Medtronic Engager™ Valve

Now Enrolling in CE Pivotal Trial

- **Self-expanding nitinol frame with self-positioning technology**
  → controlled release and accurate positioning
- **Bovine pericardial tissue valve** with supra annular valve function
- **Broad Polyester Inflow Skirt**
- **TransApical / Direct Aortic** access



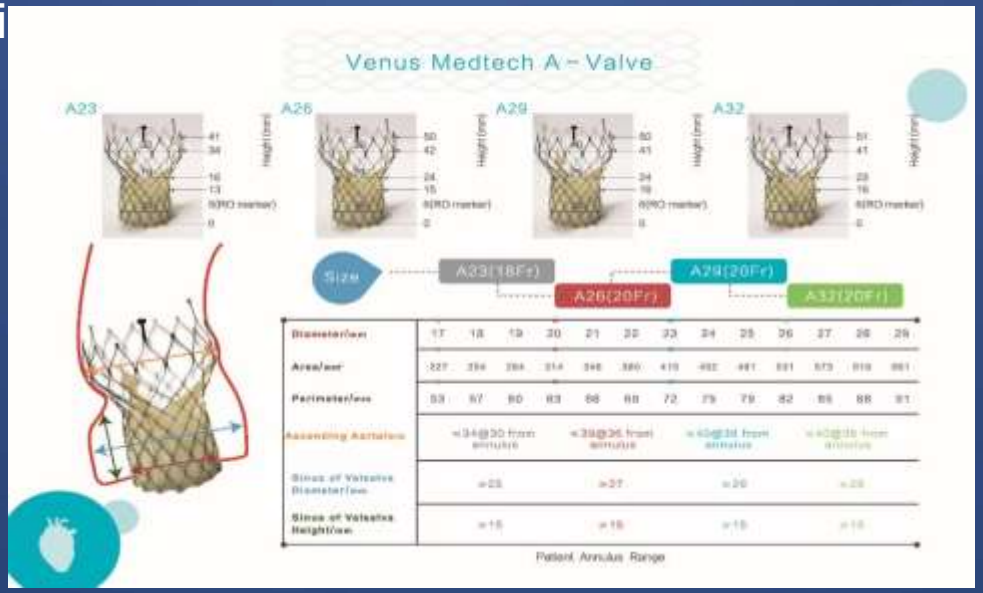
Medtronic Engager valve platform has NOT obtained CE Mark.
It is not approved in the EU or the US for commercialization.

Eur Heart J. 2011 Apr;32(7):878-87. Epub 2010 Dec 9
Methodist Debakey Cardiovasc J. 2012 Apr;8(2):9-12.

VENUS A system

- First CFDA approved THV

  (Hangzhou Venus Medtech)
- Self-expanding nitinol frame
- Porcine pericardium
- Strong radial force designed for bicuspid aortic valve and severe calcificati



Venus valve

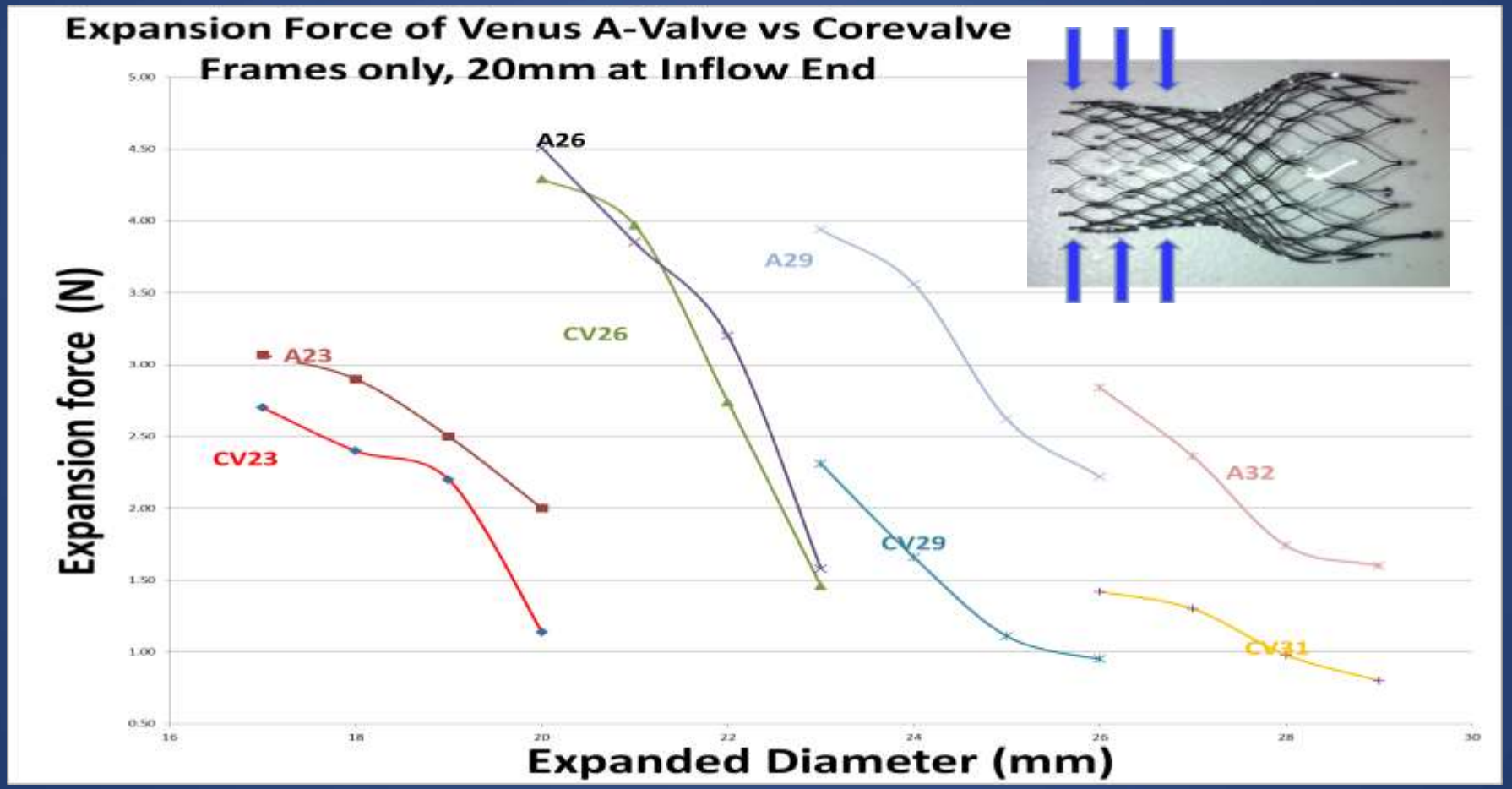
TABLE IV. 30-Day and 2-Year Outcomes

Outcome	CoreValve ($n = 27$)	Venus A-Valve ($n = 27$)	P value
30 days			
Death	1 (3.7)	1 (3.7)	1.00
Transient ischemic attack	1 (3.7)	0	–
Vascular complication			
Major	1 (3.7)	1 (3.7)	1.00
Minor	2 (7.4)	2 (7.4)	1.00
Bleeding			
Major	3 (11.1)	2 (7.4)	0.64
Minor	3 (11.1)	0	–
Aortic regurgitation ≥mild	4 (14.8)	3 (11.1)	0.69
New permanent pacemaker	10 (37.0)	2 (7.4)	0.03
2 years			
Death	3 (11.1)	2 (7.4)	0.64

Liao et al. Catheterization and cardiovascular interventions 2017;89:528-533

Venus A-Valve

Compared to Evolut R



Horst Sievert, TVT 2017

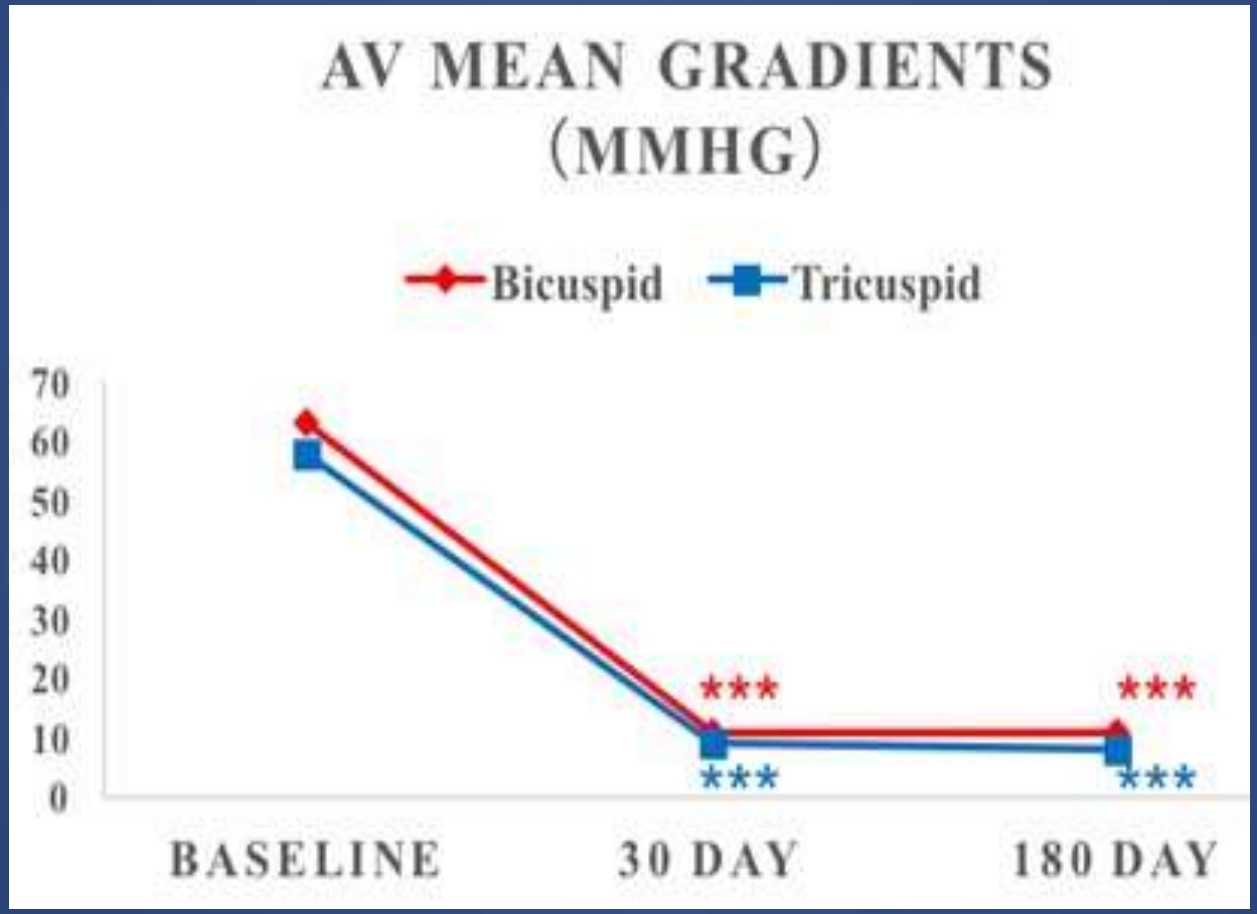
Venus A-Valve
Adverse Events

	n = 37
New onset LBBB	5 (13.5%)
New onset complete heart block	5 (13.5%)
Pacemaker implantation	10 (27%)
Acute renal failure	2 (5.4%)
Thrombocytopenia	2 (5.4%)
Puncture site bleeding	2 (5.4%)
Puncture site infection	1 (2.7%)
Coronary artery occlusion	0
Stroke (ischemic)	1(2.7%)
Pericardial effusion	0
Aortic dissection	0
Device embolization/dislodgement	1 (2.7%)
Death	3 (8.1%)

Horst Sievert, TVT 2014

Venus A-Valve in Bicuspid AV

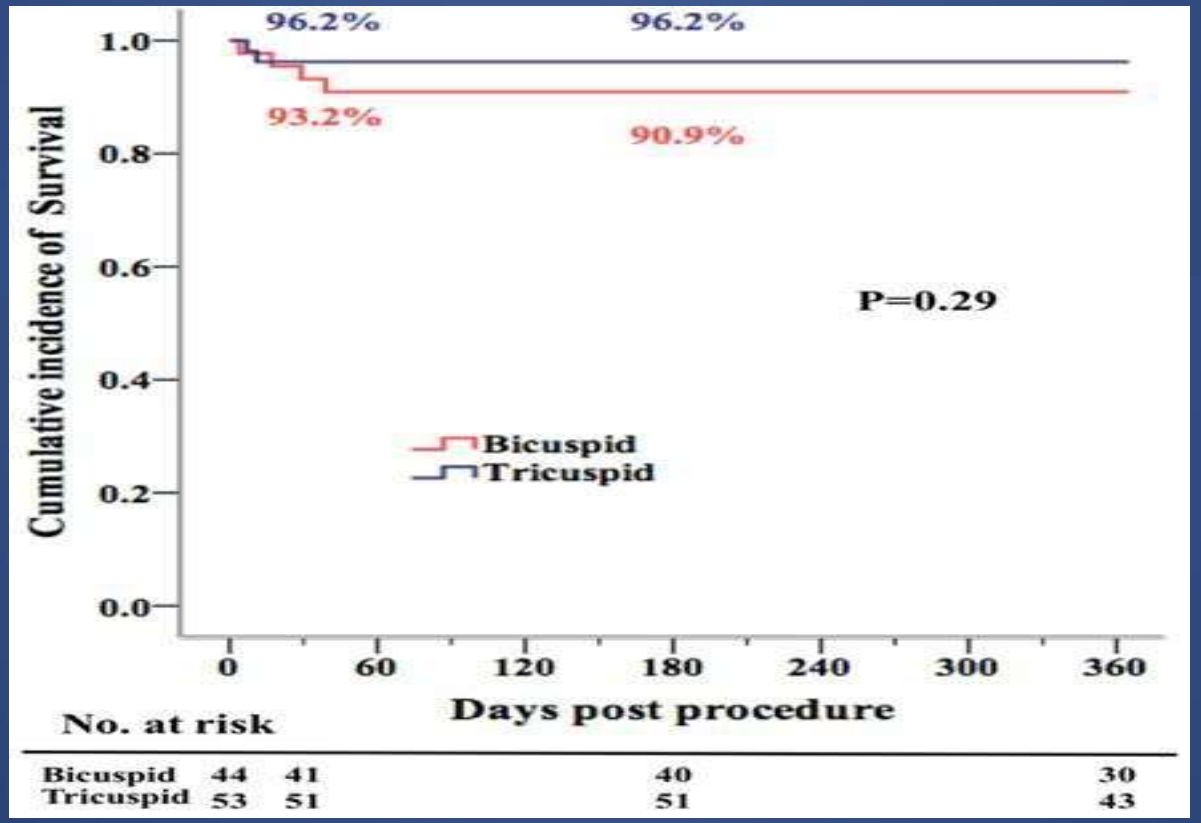
Venus-A trial



Hasan Jilaihawi, TCT 2016

Venus A-Valve in Bicuspid AV

Venus-A trial

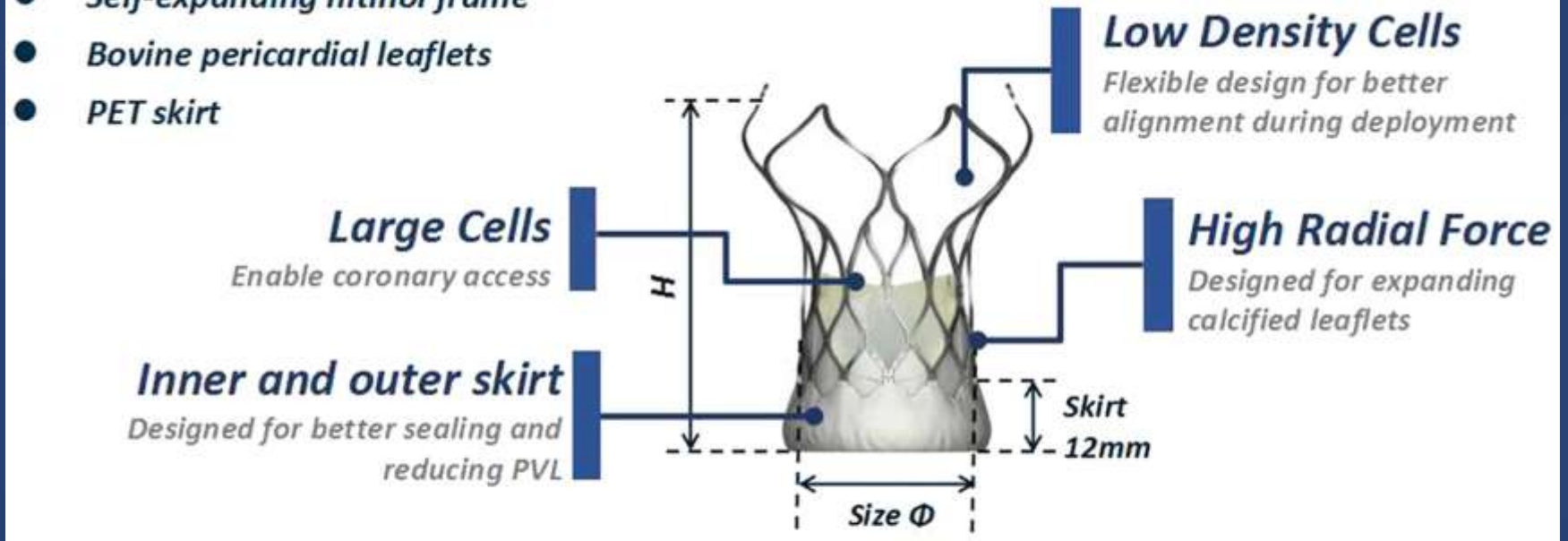


Hasan Jilaihawi, TCT 2016

VitaFlow

VitaFlow™ Aortic Valve

- *Self-expanding nitinol frame*
- *Bovine pericardial leaflets*
- *PET skirt*

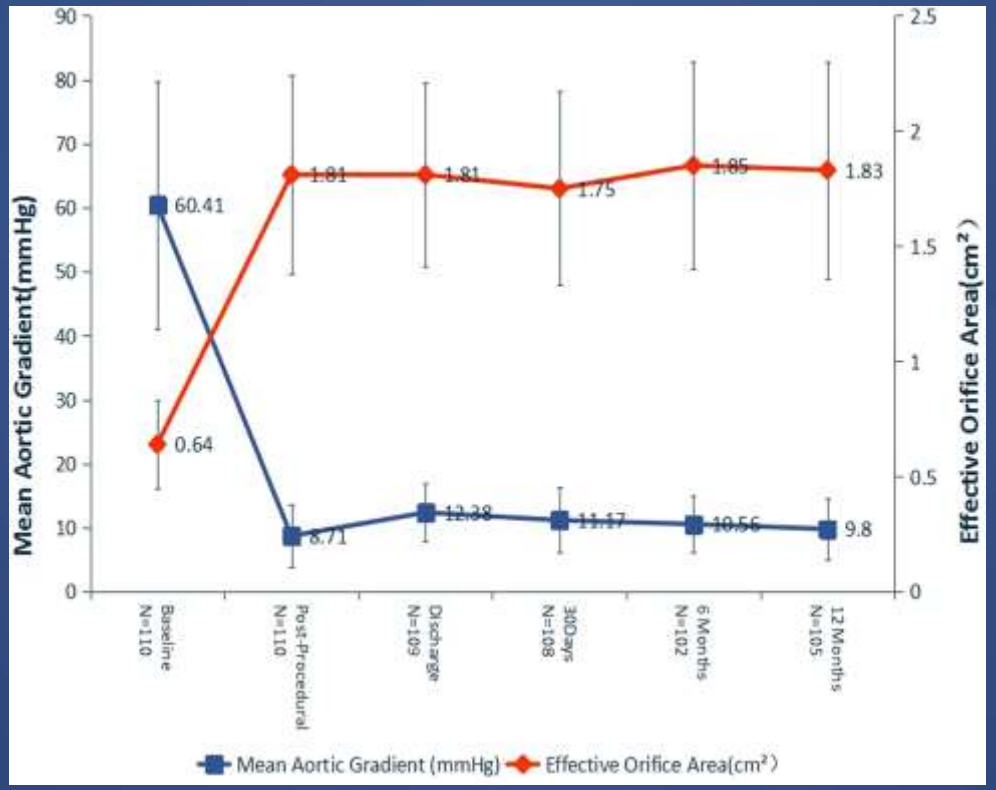


Size Φ	21mm	24mm	27mm	30mm
Aortic Annulus Diameter	17-20mm	20-23mm	23-26mm	26-29mm
Height H	50mm	50mm	53mm	53mm

Cathet Cardio Intervent, Volume: 95, Issue: 2, Pages: 332-338.

VitaFlow

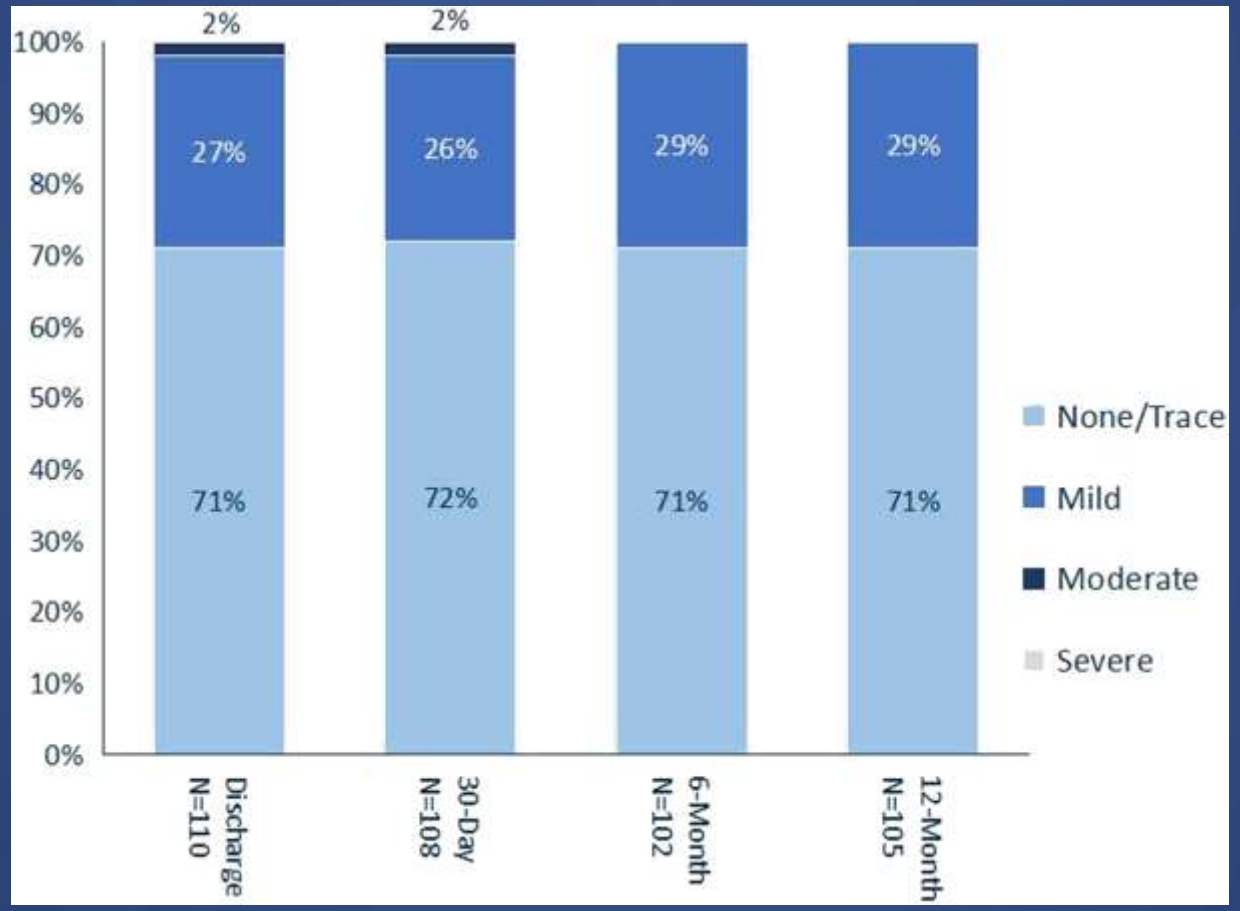
Mean aortic gradient was 9.80 ± 4.77 mmHg at 1 year
Mean effective orifice area was 1.83 ± 0.47 cm^2 at 1 year



Cathet Cardio Intervent, Volume: 95, Issue: 2, Pages: 332-338

VitaFlow

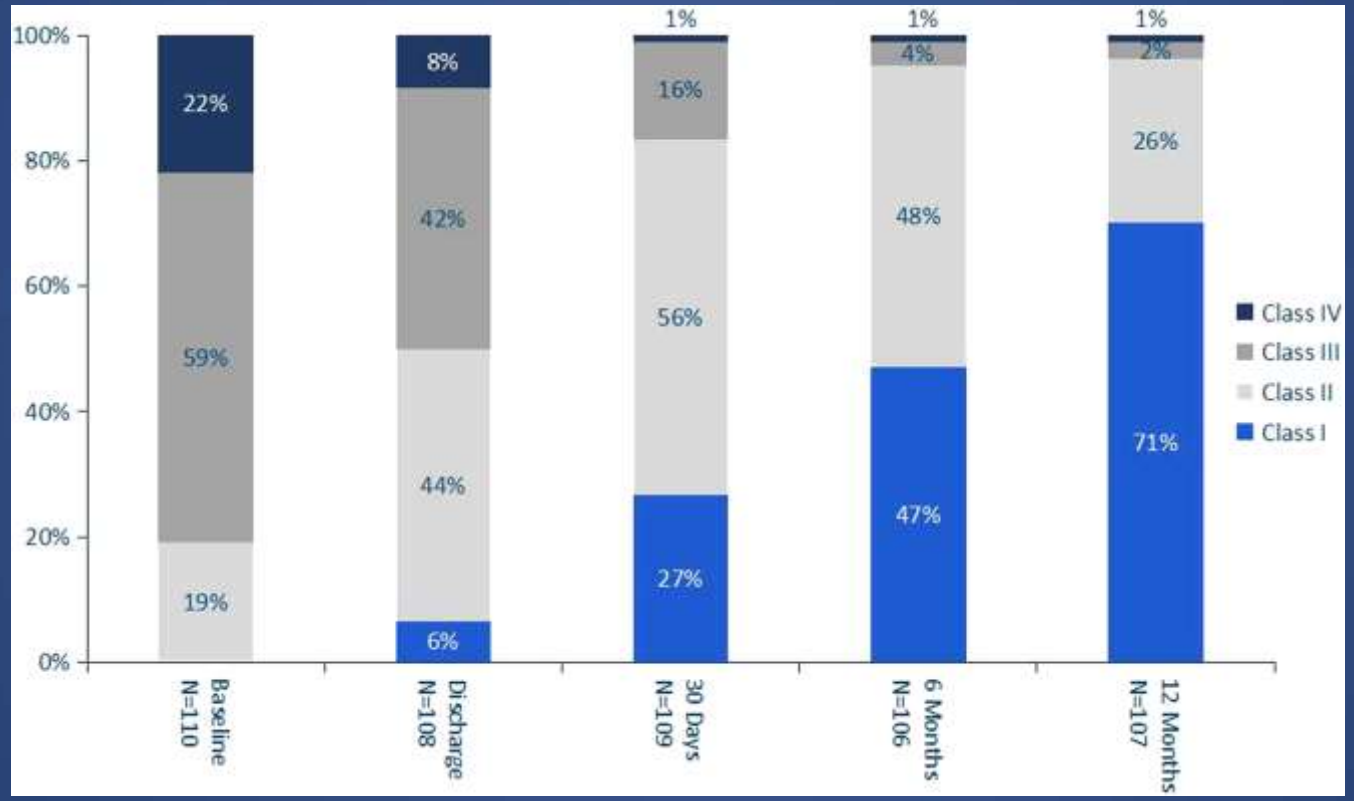
No moderate or severe PVL at 12 months



Cathet Cardio Intervent, Volume: 95, Issue: 2, Pages: 332-338

VitaFlow

Ninety-seven percent of patients achieved NYHA ≤ II



Cathet Cardio Intervent, Volume: 95, Issue: 2, Pages: 332-338

VitaFlow

Similar outcomes in bicuspid aortic valves and tricuspid aortic valve

Clinical outcomes	Tricuspid *N* = 68	Bicuspid *N* = 42	*p* Value
All-cause mortality (%)	4.4%	0.0%	.285
Cardiovascular mortality	2.9%	0.0%	.524
Procedure success rate (%)	88.2	90.4	1.000
All stroke (Major and Minor; %)	4.6%	4.8%	1.000
Major vascular complication (%)	4.5%	0.0%	.158
Moderate or severe PVL (%)	0.0%	0.0%	1.000
New pacemaker implantation (%)	22.1%	14.3%	.454
Mean aortic gradient (mmHg)	9.62 ± 4.75	9.92 ± 4.78	1.000
Aortic valve area (cm^2)	1.84 ± 0.48	1.82 ± 0.47	1.000
NYHA class I(%)	67.7%	73.8%	.631

Cathet Cardio Intervent, Volume: 95, Issue: 2, Pages: 332-338

VitaFlow Library

- Hybrid density stent with double-layer skirts
- Bovine pericardial leaflet
- Retrievable delivery system
  - Motorized handle
  - Allowed for fast, stable, and accurate release and retrieval
- The delivery system whose distal end can be bent 360 degrees
  - Providing superior flexibility to help minimize blood vessel damage
  - Reducing the risk of complications

Cathet Cardio Intervent, Volume: 95, Issue: 2, Pages: 332-338.

Mechanically-expandable valves

Direct Flow Medical Aortic valve

- 2 sizes matching valvuloplasty balloons
- Conformable cuff design and precise positioning
  → Reduces PV Leaks and AI
- “Surgical” valve design
- Repositionable & Removable
- Immediately competent
- Valve design allows hemodynamic assessment prior to final device deployment

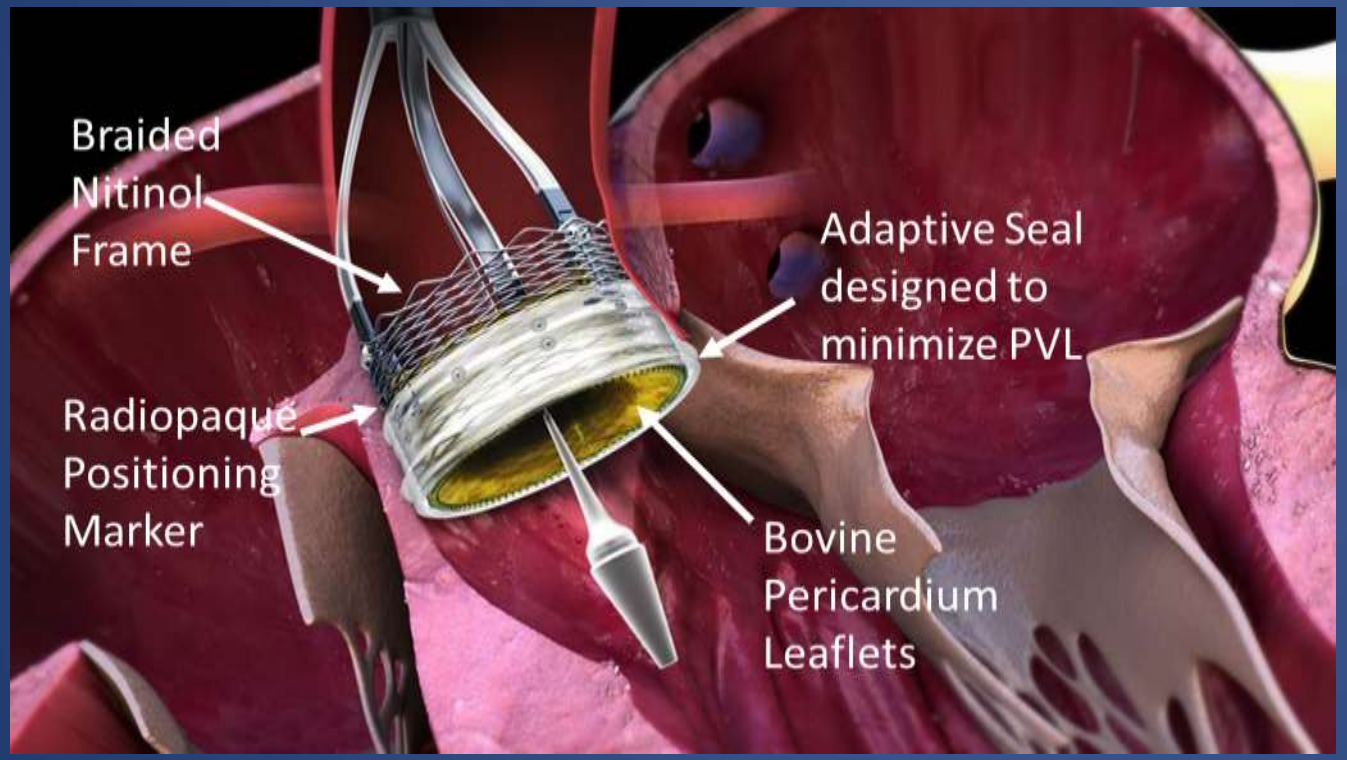
* CE approval, anticipated at the end of 2012

Methodist Debakey Cardiovasc J. 2012 Apr;8(2):9-12

Direct Flow Medical Aortic valve

REPRISE III

The LOTUS Valve



- Controlled mechanical expansion; rapid pacing not needed during deployment
- Early valve function; hemodynamic stability during implantation
- Complete assessment before release; reposition/retrieve if not acceptable

REPRISE III
Lotus Valve System

REPRISE III Study Design

Severe aortic stenosis; extreme or high operative risk
Annulus ≥20 mm and ≤27 mm; transfemoral access

Heart Team assessment → Case Review Committee confirmation

Randomised 2:1 (LOTUS : CoreValve)
N=912

Neurologist examination‡

- **LOTUS Valve*** (23, 25 & 27mm)
- **CoreValve†** (26, 29 & 31mm)

- DAPT ≥1m *OR* warfarin + ASA or clopidogrel ≥1m (if anticoagulation needed)
- Clinical & echocardiographic follow-up: discharge or 7d, 30d, 6m, annually 1-5y

* Performed by a neurologist, neurology fellow, neurology physician assistant, or neurology nurse practitioner
† CoreValve platform (includes CoreValve Classic and Evolut R)
‡ Centres with no LOTUS experience enrolled 2 roll-in patients before commencing enrollment of the evaluable cohort

Endpoints

1° Safety ✓ Satisfied noninferiority
$P_{noninferiority} = 0.003$

30-day all-cause mortality, stroke, life-threatening/major bleeding, stage 2/3 AKI, major vascular complications

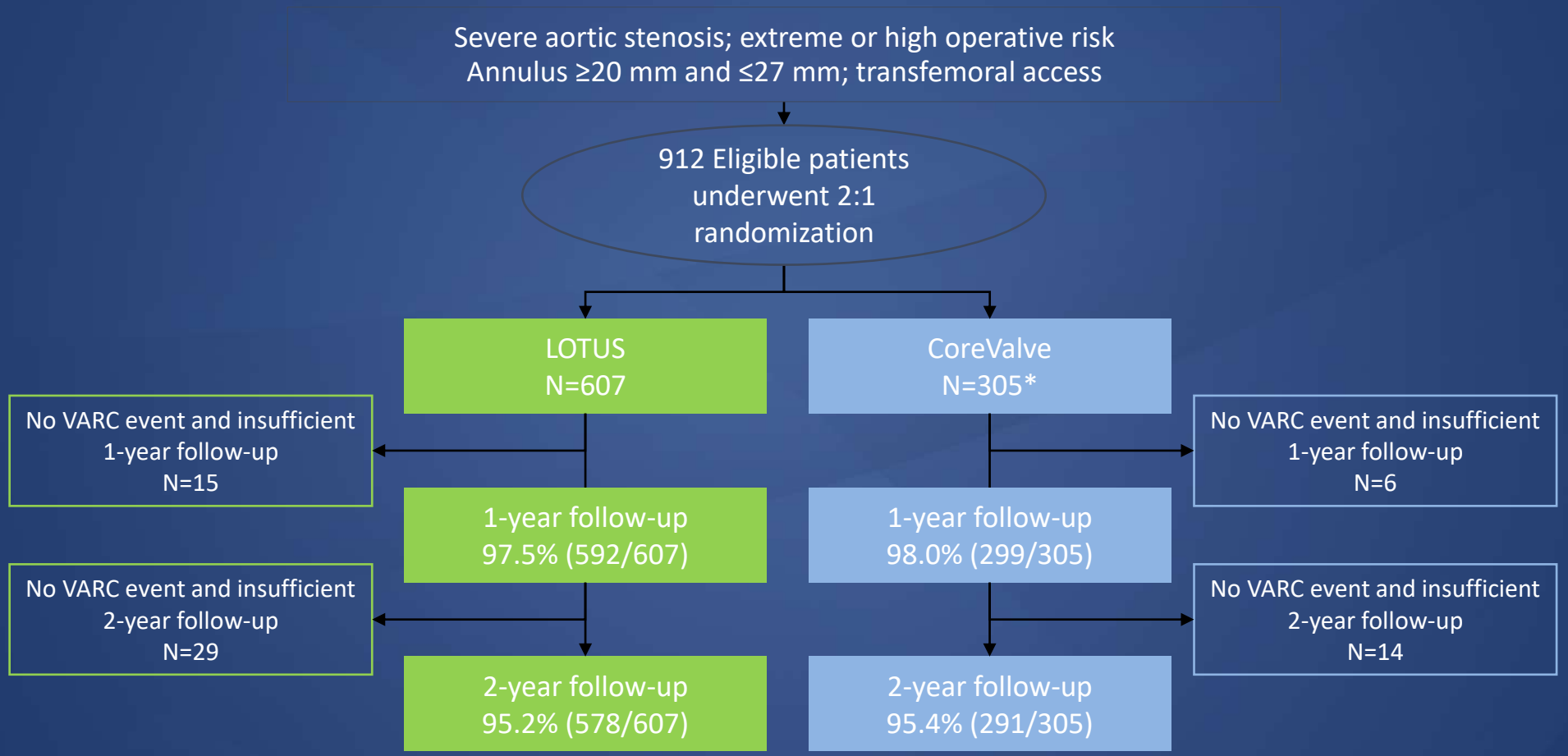
1° Effectiveness ✓ Satisfied superiority
$P_{superiority} < 0.001$

1-year Death, Disabling Stroke, ≥ Moderate PVL

Driven by significant differences in ≥moderate PVL (CoreValve 6.8% vs LOTUS 0.9%, P<0.001) and disabling stroke (7.1% vs 3.6%, P=0.02)

1Feldman TE, Reardon MJ, Rajagopal V,, et.aAl.. JAMA. 2018;319:27–37.

REPRISE III Patient Flow



*CV Classic N=153; Evolut R N=144

1Feldman TE, Reardon MJ, Rajagopal V,, et.aAl.. JAMA. 2018;319:27–37.

REPRISE III
Lotus Valve System

2 Year End Points

Key endpoints

- All cause mortality
- All cause mortality or disabling stroke

Other Clinical Outcomes

- All Stroke
- Disabling Stroke
- Repeat procedures
- Hospitalization
- Valve Thrombosis
- Pacer maker implantation

Echocardiography Outcomes

- EOA
- Mean Gradient
- PVL

Functional Outcome

- NYHA

REPRISE III
Lotus Valve System

Key Baseline Characteristics

Demographics & Comorbidities			Echocardiography		
	CoreValve (N = 305)	LOTUS (N = 607)		CoreValve (N = 305)	LOTUS (N = 607)
Age, years	82.9±7.6	82.8±7.1	Aortic valve area (cm^2)	0.70±0.19 (280)	0.69±0.19 (541)
Female sex, %	52.1	50.1	Mod/Sev Aortic regurgitation, %	8.0 (289)	6.5 (558)
STS score, %	6.9±4.1	6.7±4.0	Mean aortic gradient (mmHg)	43.9±12.3 (294)	44.6±13.4 (575)
Atrial fibrillation, %	31.6	35.1	Peak aortic gradient (mmHg)	72.4±18.1 (294)	73.6±20.8 (575)
Pacemaker, %	19.0	17.8	Mod/Sev Mitral regurgitation, %	11.7 (283)	10.7 (554)
Prior stroke, %	14.5	11.3	LVEF (%)	55.9±11.8 (254)	56.1±11.4 (485)

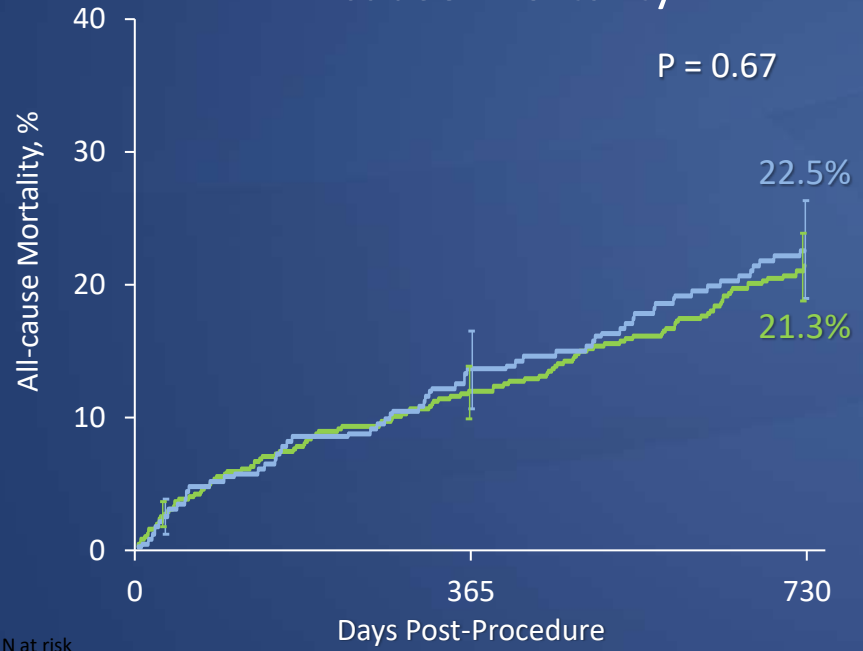
1Feldman TE, Reardon MJ, Rajagopal V,, et.aAl.. JAMA. 2018;319:27–37.

Key Endpoints – REPRISE III

2 Year – Intent-to-Treat

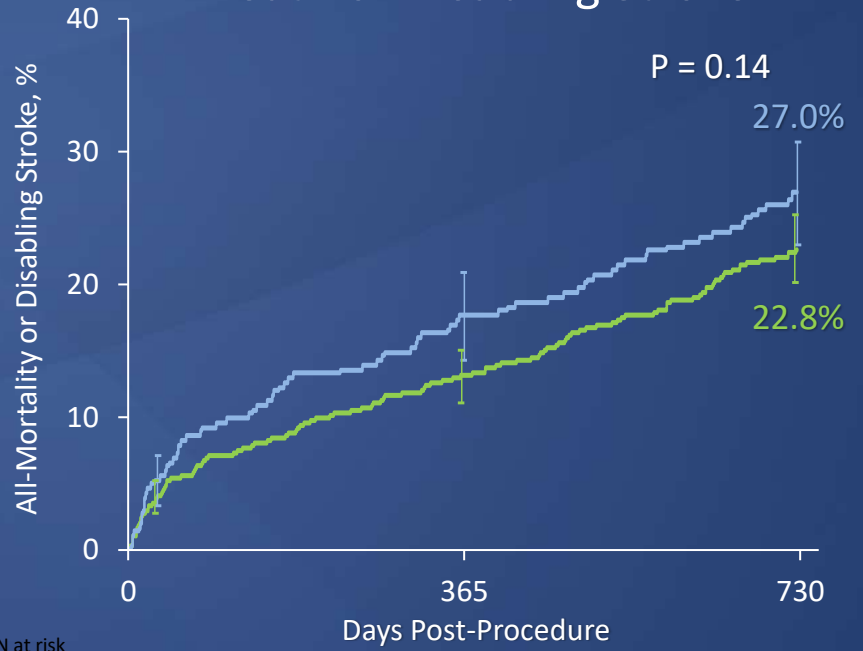
CoreValve
LOTUS

All-cause Mortality



N at risk			
CoreValve	302	264	200
LOTUS	596	531	423

Death or Disabling Stroke



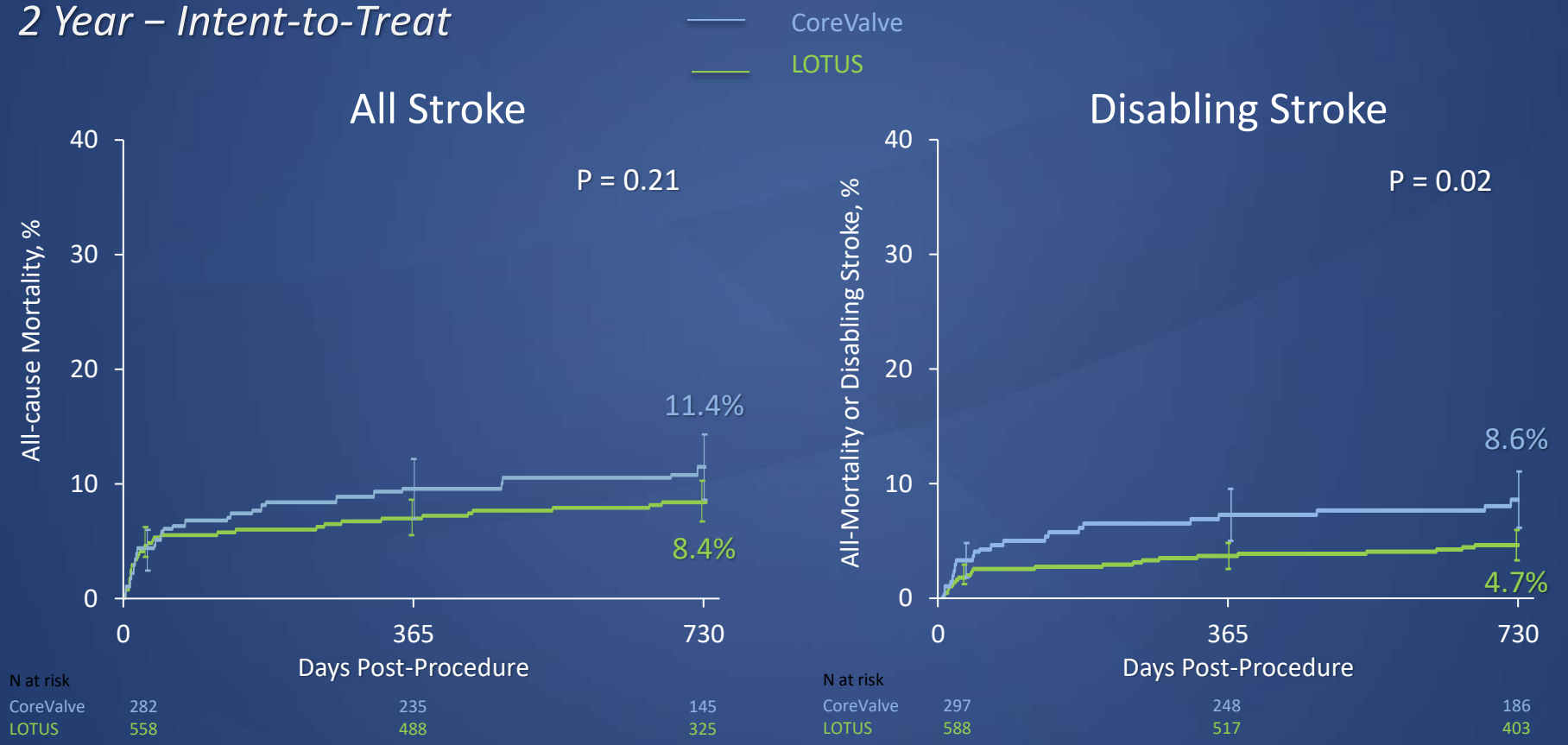
N at risk			
CoreValve	299	252	193
LOTUS	591	522	416

ITT; KM Event Rate ± 1.5 SE; log-rank *P* value

CV=CoreValve

Other Clinical Outcomes

2 Year – Intent-to-Treat

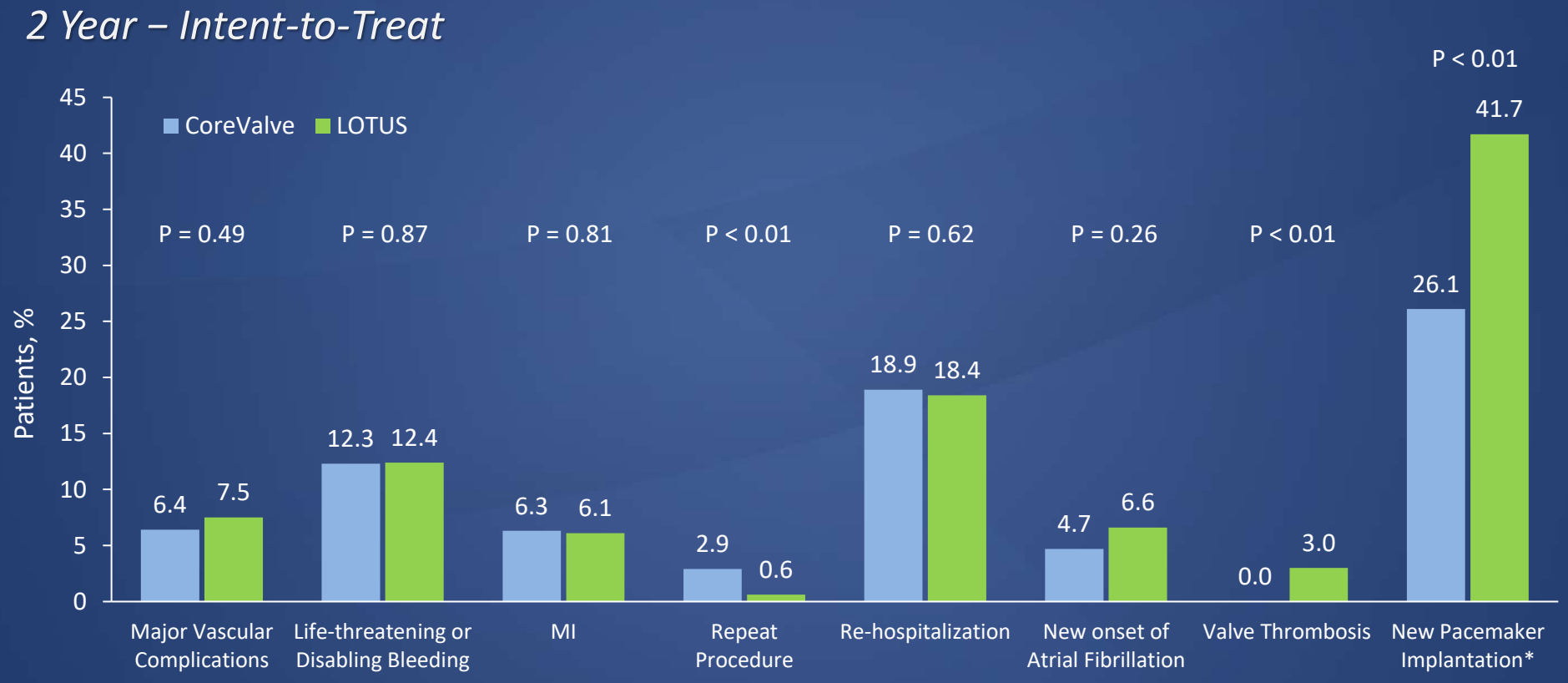


ITT; KM Event Rate ± 1.5 SE; log-rank *P* value

CV=CoreValve

REPRISE III
Lotus Valve System

Additional VARC Events at 2 Years



*New Pacemaker implantation rate excludes patients with a prior pacemaker
ITT; KM Event Rate; log-rank P value; Re-hospitalization for valve-related symptoms or worsening congestive heart failure (NYHA class III or IV);

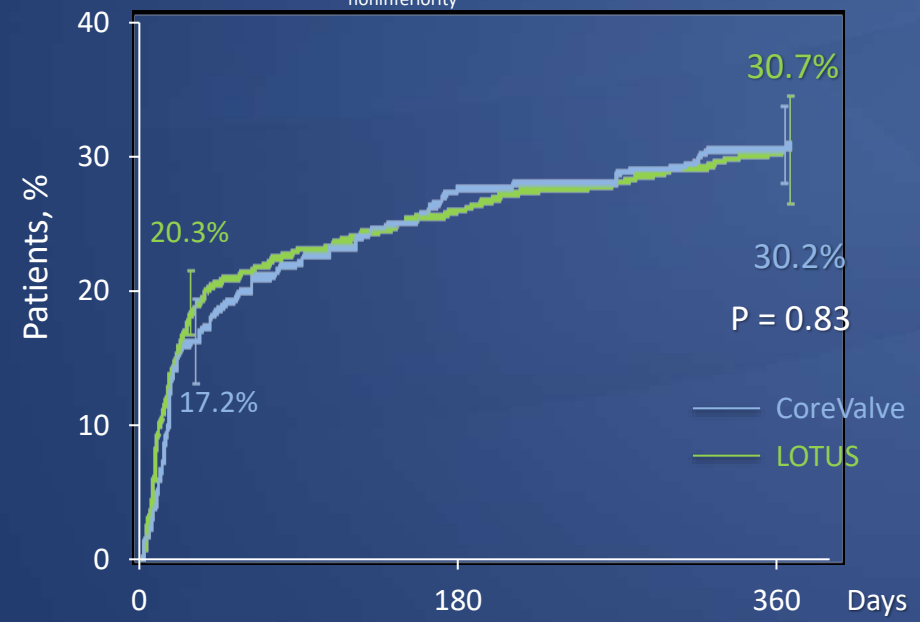
REPRISE III – Primary Results

Primary Composite Safety Endpoint

30-day All-cause mortality, stroke, life-threatening/major bleed, stage 2/3 AKI, major vascular complications

✓ Satisfied noninferiority

$P_{noninferiority} = 0.003$



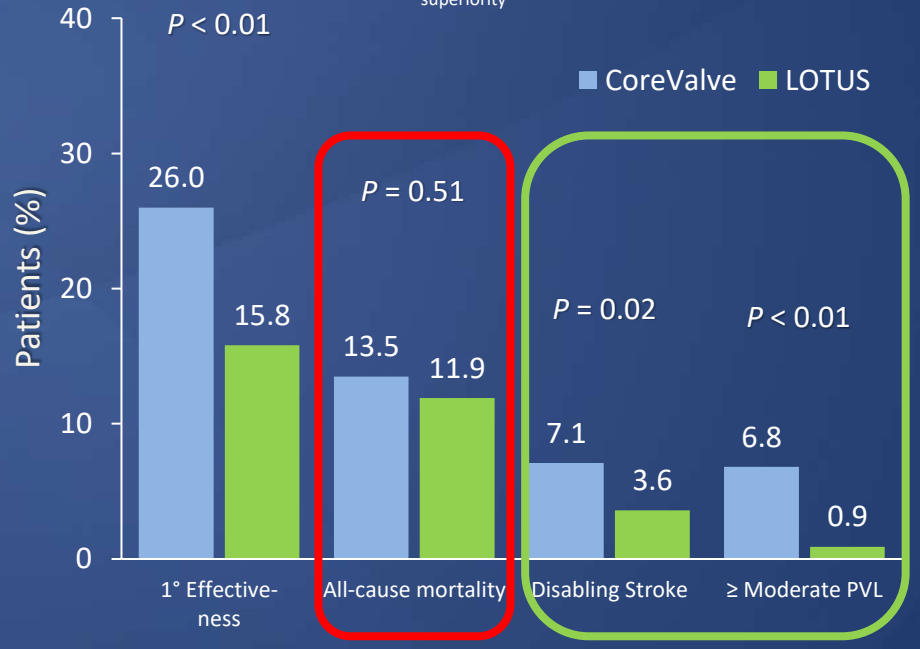
Implanted; KM Event Rate ± 1.5 SE; log-rank *P* value

Primary Effectiveness Endpoint

1-year Death, Disabling Stroke, Moderate or Greater PVL

✓ Satisfied superiority

$P_{superiority} < 0.001$



ITT; Binary event rates; P-value from Chi square test

Feldman et al, *JAMA* 2018

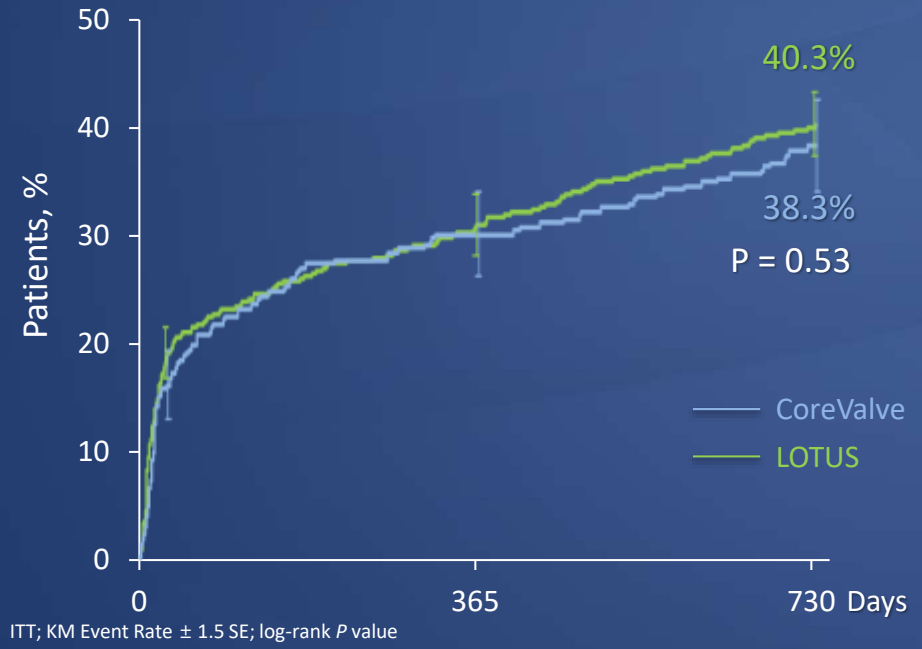
REPRISE III
Lotus Valve System

Primary Safety and Effectiveness at 2 years

Intent-to-Treat

Primary Composite Safety Endpoint

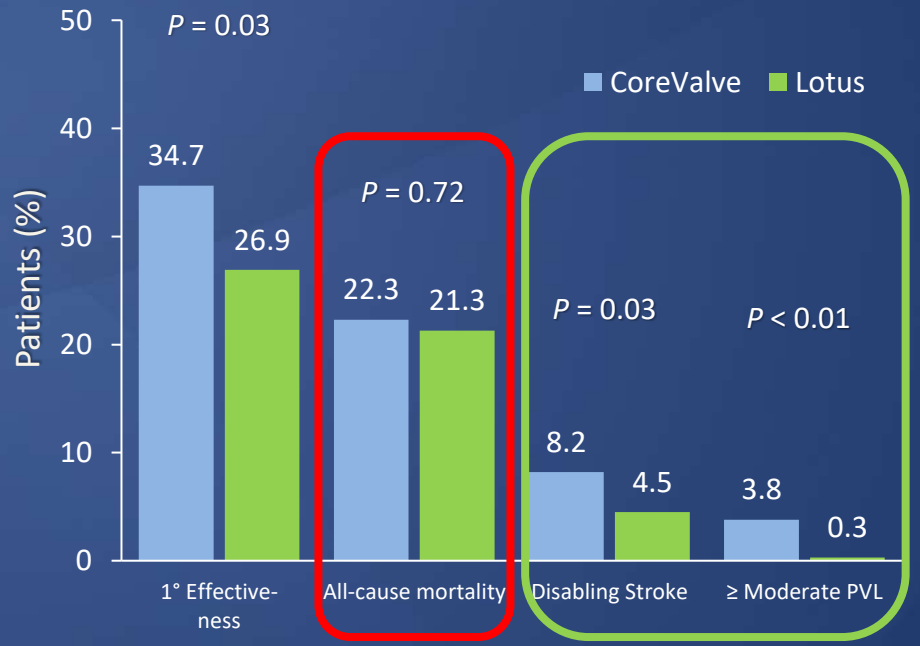
All-cause mortality, stroke, life-threatening/major bleed, stage 2/3 AKI, major vascular complications



ITT; KM Event Rate ± 1.5 SE; log-rank *P* value

Primary Effectiveness Endpoint

Death, Disabling Stroke, Moderate or Greater PVL



ITT; Binary event rates; P-value from Chi square test

REPRISE III
Lotus Valve System

Hemodynamics

Core Lab Data

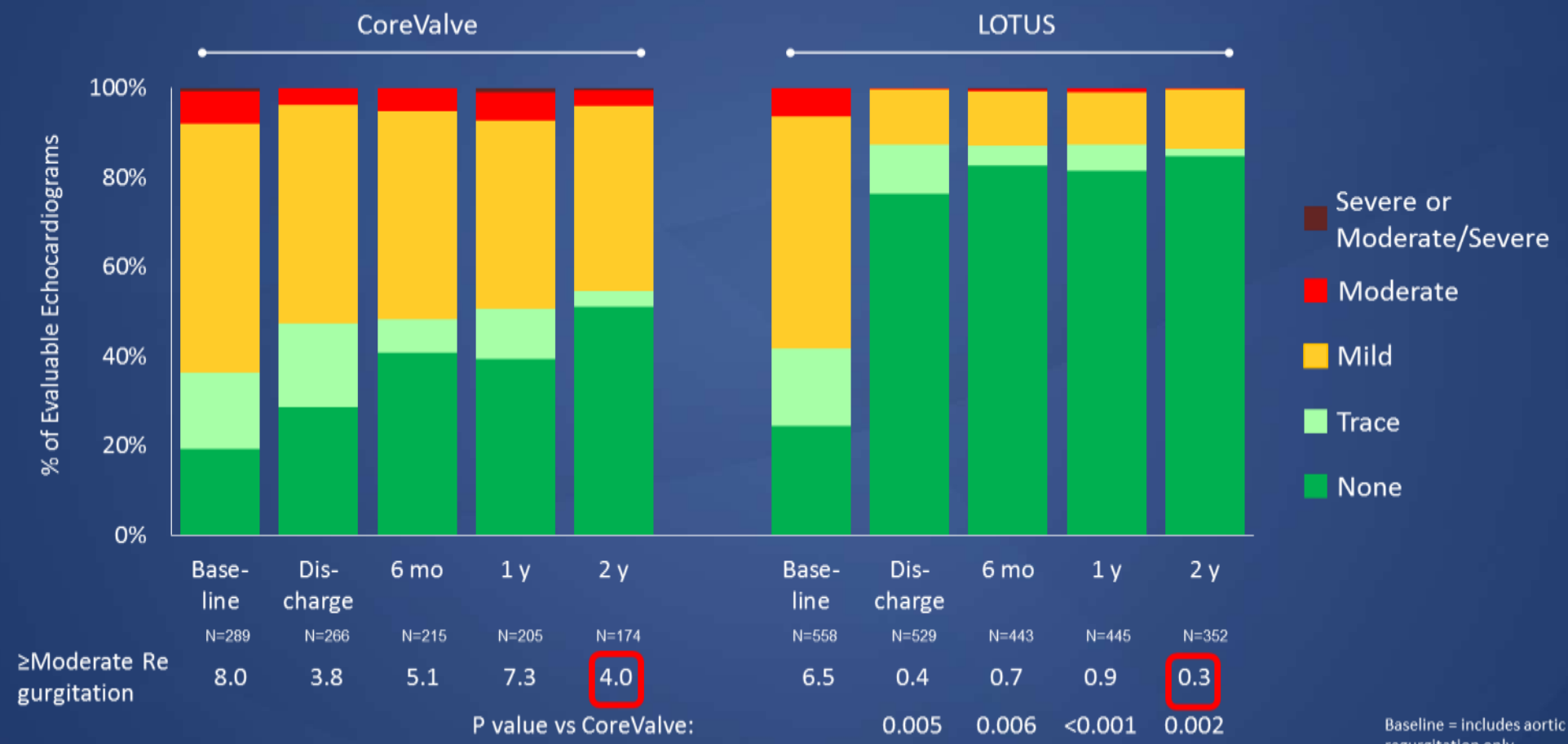
		Baseline	Discharge	6 months	1 year	2 years
Mean Gradient	CoreValve (N)	294	280	234	220	176
	LOTUS (N)	575	564	485	465	381
EOA	CoreValve (N)	280	246	210	200	167
	LOTUS (N)	541	510	440	422	326

LOTUS vs CoreValve: *P* <0.001 at discharge and later time points

Values are mean±SD; intent-to-treat analysis set

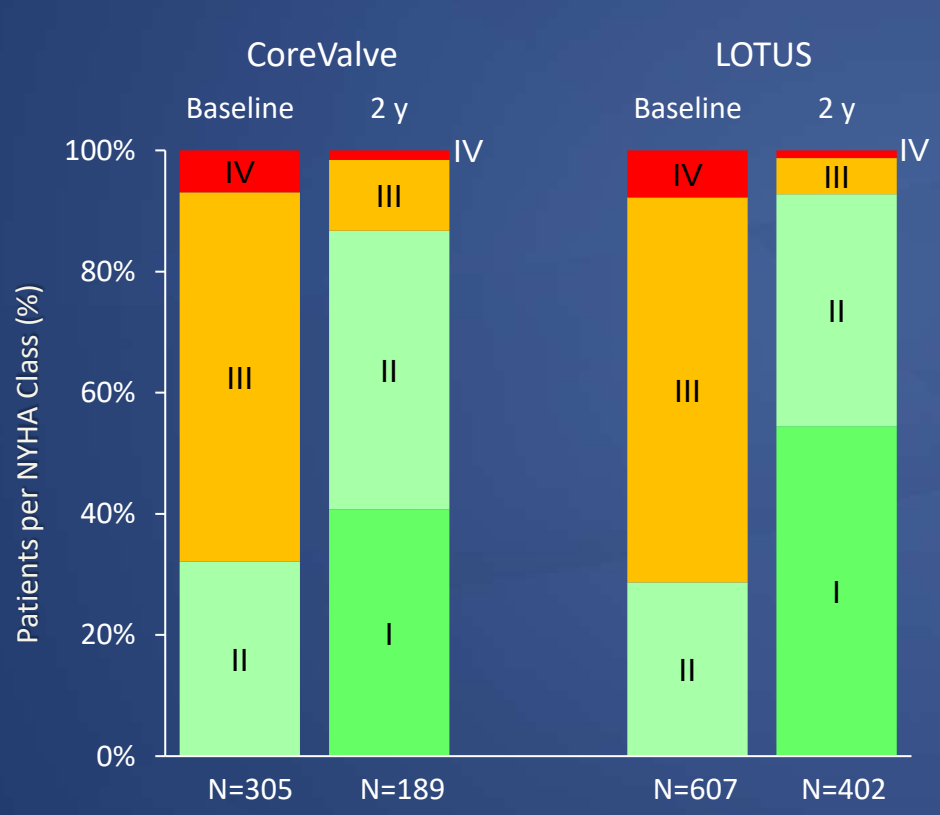
REPRISE III
Lotus Valve System

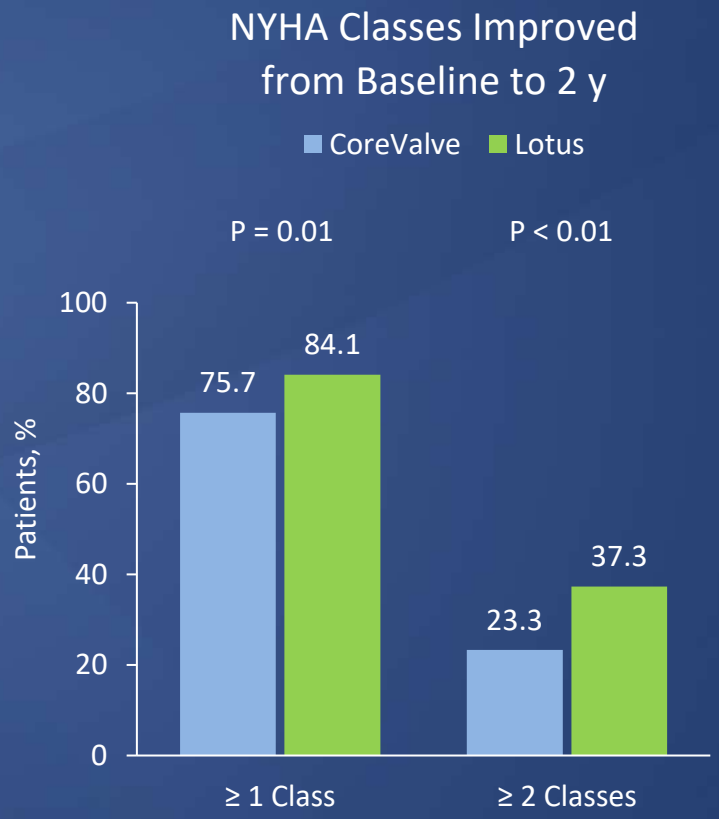
Regurgitation through 2 years



Baseline = includes aortic regurgitation only

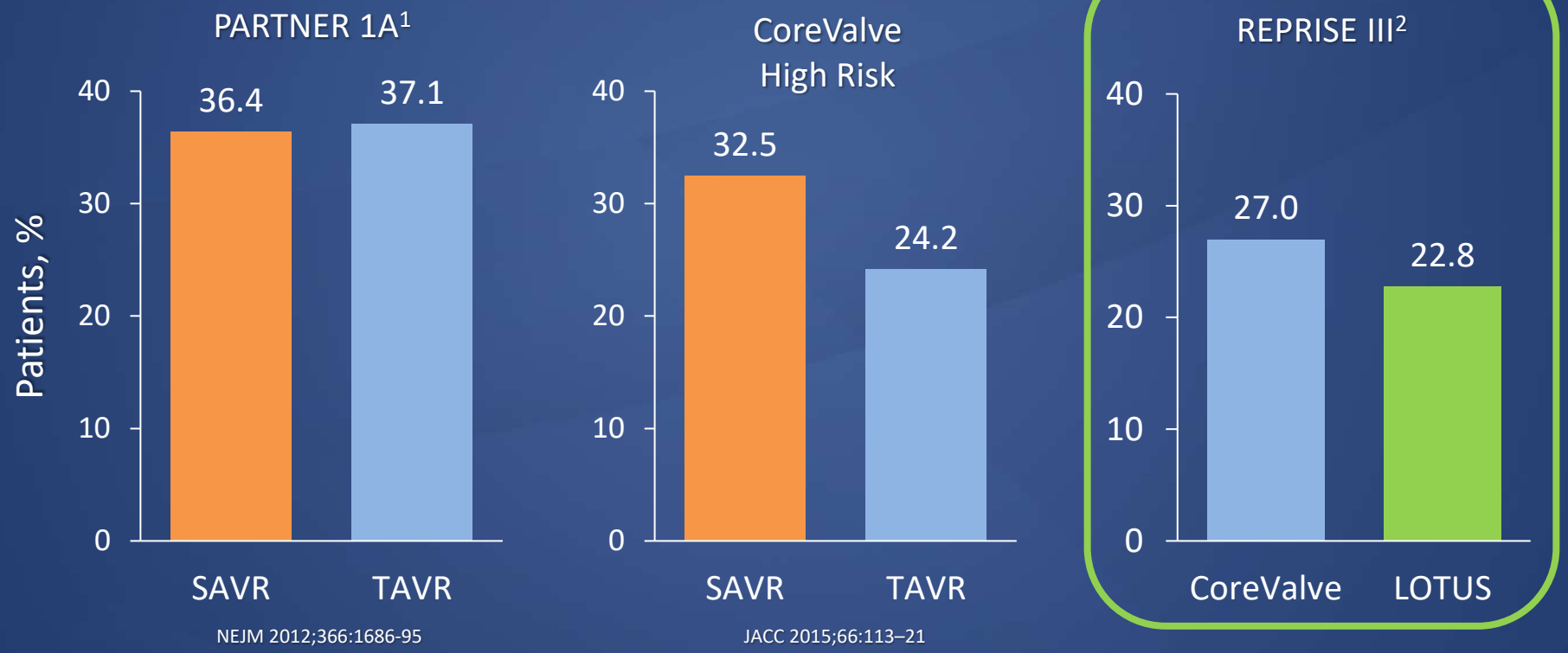
Functional Status at 2 years





High Risk TAVR Randomized Trials

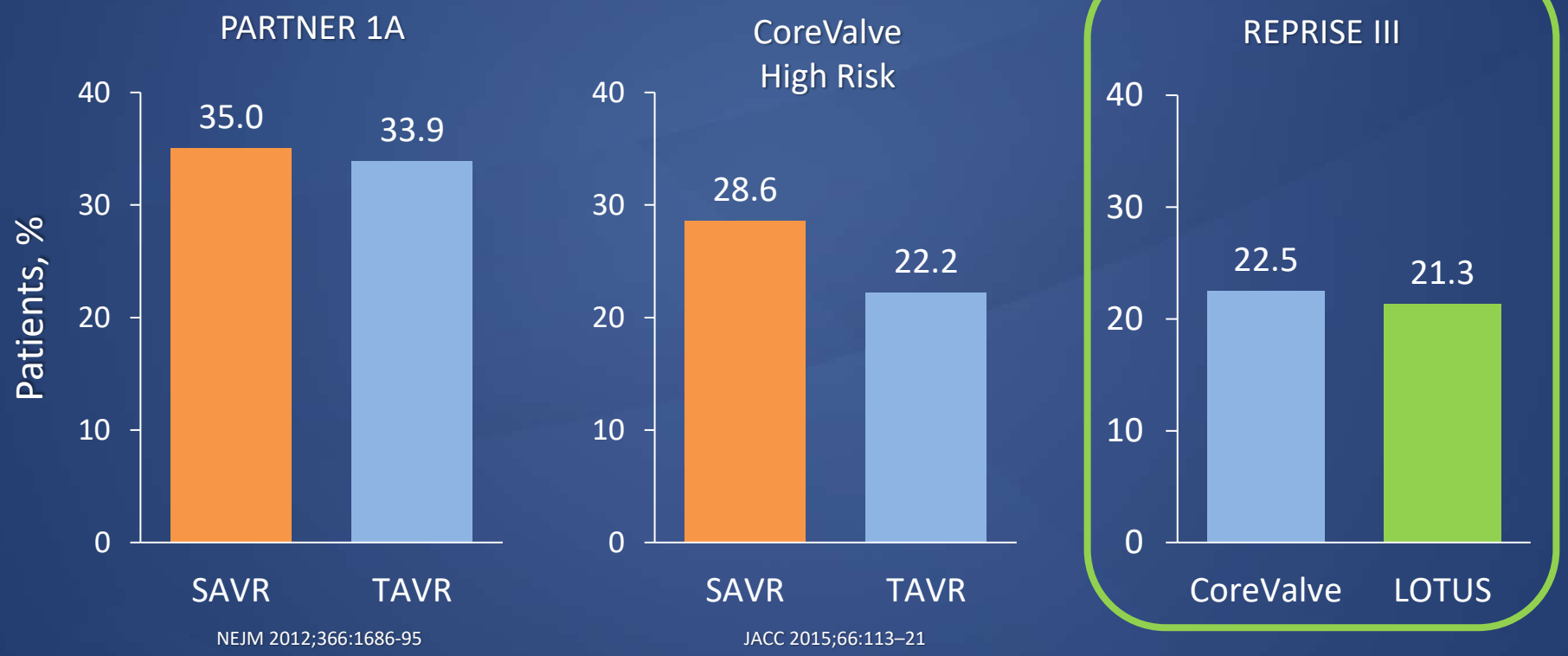
Death and Disabling Stroke at 2 years



[1]Death or all stroke; [2]Neurologic examinations were performed by a neurology specialist following any suspected stroke

High Risk TAVR Randomized Trials

Death at 2 years



Conclusions

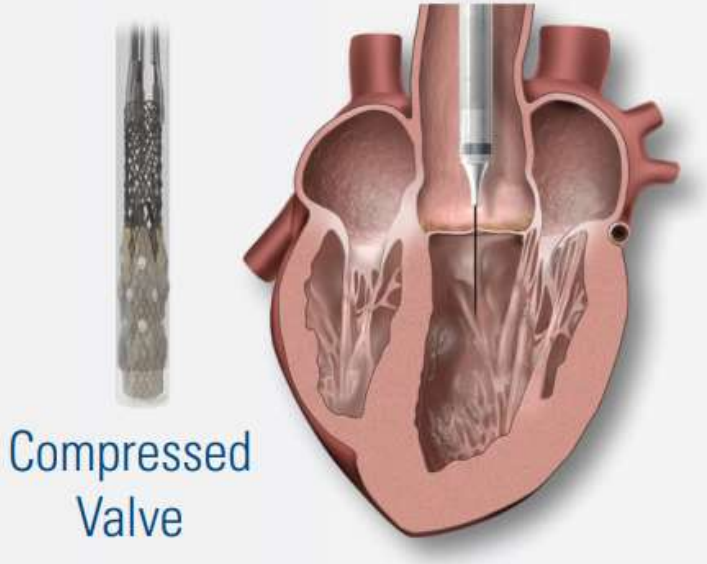
The 2-year findings in REPRISE III continue to demonstrate the safety and effectiveness of the LOTUS valve

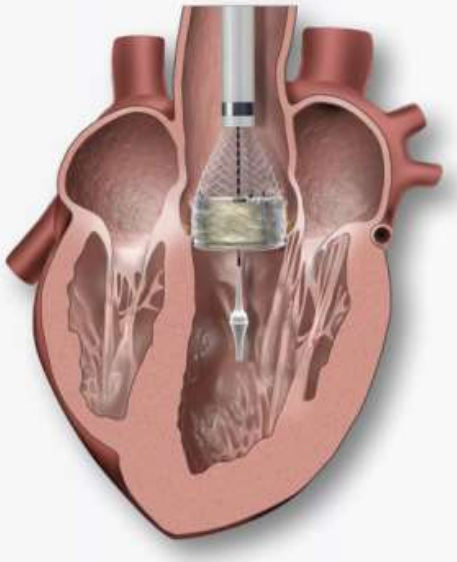
- At 2 years compared to CoreValve LOTUS patients experienced:
  - Less moderate or greater paravalvular leak
  - Fewer disabling strokes
  - Fewer repeat procedures
  - More valve thrombosis
  - More new pacemaker implantations
  - Smaller valve areas and higher gradients
- At 2 years, more LOTUS patients had improvements in NYHA class compared to CoreValve
- Ongoing follow-up will provide safety and performance information on the LOTUS valve to at least 5 years

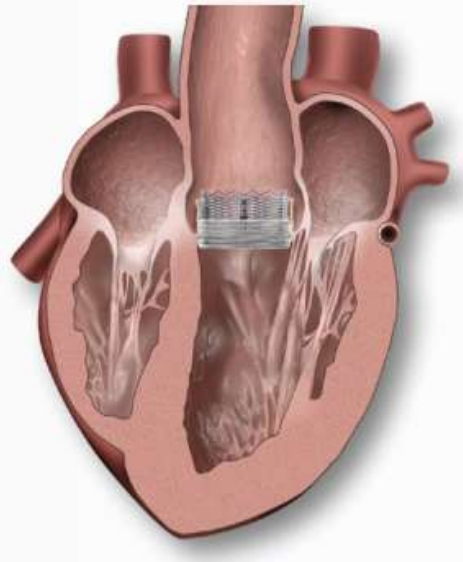
The LOTUS *Edge*™

- 100% repositionable
- Adaptive Seal around the outside of the valve frame to help reduce PVL

The LOTUS *Edge*™







Step 1

The artificial valve is compressed onto a catheter that travels through the body to the heart, inside of a large blood vessel that leads to the diseased aortic valve.

Step 2

The physician expands the replacement valve, pushing the diseased parts of the aortic valve out of the way

Step 3

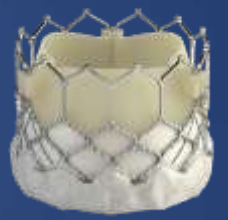
The new valve begins to function immediately and restore healthy blood flow. Once the valve is in place, the physician removes the catheter, closes the incision, and the procedure is complete

ViV: Mitral Valve

MITRAL Trial
Mitral Implantation of TRAnscatheter vaLves

90 patients extremely high surgical risk (STS PROM >15% or M&M >50%)

SAPIEN XT



SAPIEN 3

Inclusion Criteria

NYHA II or greater

Native MV (MAC) n=30

Severe MS (MVA ≤1.5 cm2)
Severe MR + Moderate MS

Results of MViMAC
Presented at TCT
Nov 1st, 2017

Valve-in-Ring n=30

Severe MS (MVA ≤1.5 cm2)
At least Moderate-Severe MR

Results of MViR
Presented at TCT
Nov 1st, 2017

Valve-in-Valve n=30

Severe MS (MVA ≤1.5 cm2)
At least Moderate-Severe MR

Results of MViV
Presented at AHA
Nov 13th, 2017

Mayra Guerrero, TVT 2018

MITRAL Trial

Valve-in-Valve Arm

Valve Type	n
Edwards Perimount Family (Perimount, Magna Ease, Baxter)	16
Edwards CE Standard	3
Medtronic Mosaic	6
St. Jude Biocor/Epic	5

38 patients presented in case review call* → 8 patients excluded:
- 3= RV dysfunction
- 2= Became unstable requiring pressors
- 1= No central MR, mostly PVL
- 1= EF barely 20%, cohort "C"
- 1= Risk of LVOTO

↓

30 patients enrolled

↓

30 patients treated

Failure mode	n(%)
Stenosis	18 (60%)
Regurgitation	8 (26.7%)
Both	4 (13.3%)

*All patients presented at case review call
All CT scans reviewed by Core Lab prior to presentation

Last implant 10-17-17
Not all data monitored yet
(this is a preliminary analysis)

Mayra Guerrero, TVT 2018

MITRAL Trial

Mitral ViV Procedural Outcomes

100% Transseptal access

Outcomes	In-Hospital n=30	30 Days n=30
All-Cause Mortality	**0**	1 (3.3%)
Cardiovascular death	**0**	**0**
Non-Cardiac death	**0**	1 (3.3%) Asphyxia due to chocking at home on POD #29 after taking 6 pills at same time (confirmed by autopsy)

Data not yet adjudicated, may be subject to change.

Mayra Guerrero, TVT 2018

MITRAL Trial

Mitral ViV Primary Safety Endpoints

	n=30
Technical success at exit from Cath Lab	**30 (100%)**
Procedural Success at 30 days	**27 (90%)**
Death at 30 days	1 (3.3%)
MVA < 1.5 cm2	2 (6.7%)

Mayra Guerrero, TVT 2018

MITRAL Trial

Intraprocedural or In-Hospital Complications

	ViV n=30 n (%)
Valve embolization	0
LVOT Obstruction with hemodynamic compromise	0
Left ventricular perforation	0
Pericardial effusion requiring pericardiocentesis	0
Conversion to open heart surgery during index procedure	0
Paravalvular leak closure	0
Myocardial infarction requiring intervention	0
Stroke	0
New pacemaker	**1 (3.3%)**
Blood transfusion (GU bleed)	**1 (3.3%)**
Vascular complications (hematoma=3)	**3 (10%)**

Mayra Guerrero, TVT 2018

MITRAL Trial

Echocardiogram at 30 days

	ViV n=29*
Ejection Fraction (%)	51.1 (±12.4)
Mean MVG (mmHg)	5.8 (±2.13)
MVA (cm2)	1.86 (±0.68)
Peak LVOT gradient (mmHg)	6.9 (±6.1)
Mitral Regurgitation	
None or Trace	29 (100%)
1 (+)	0
2(+)	0
≥3 (+)	0

* 1 patient died on POD #29

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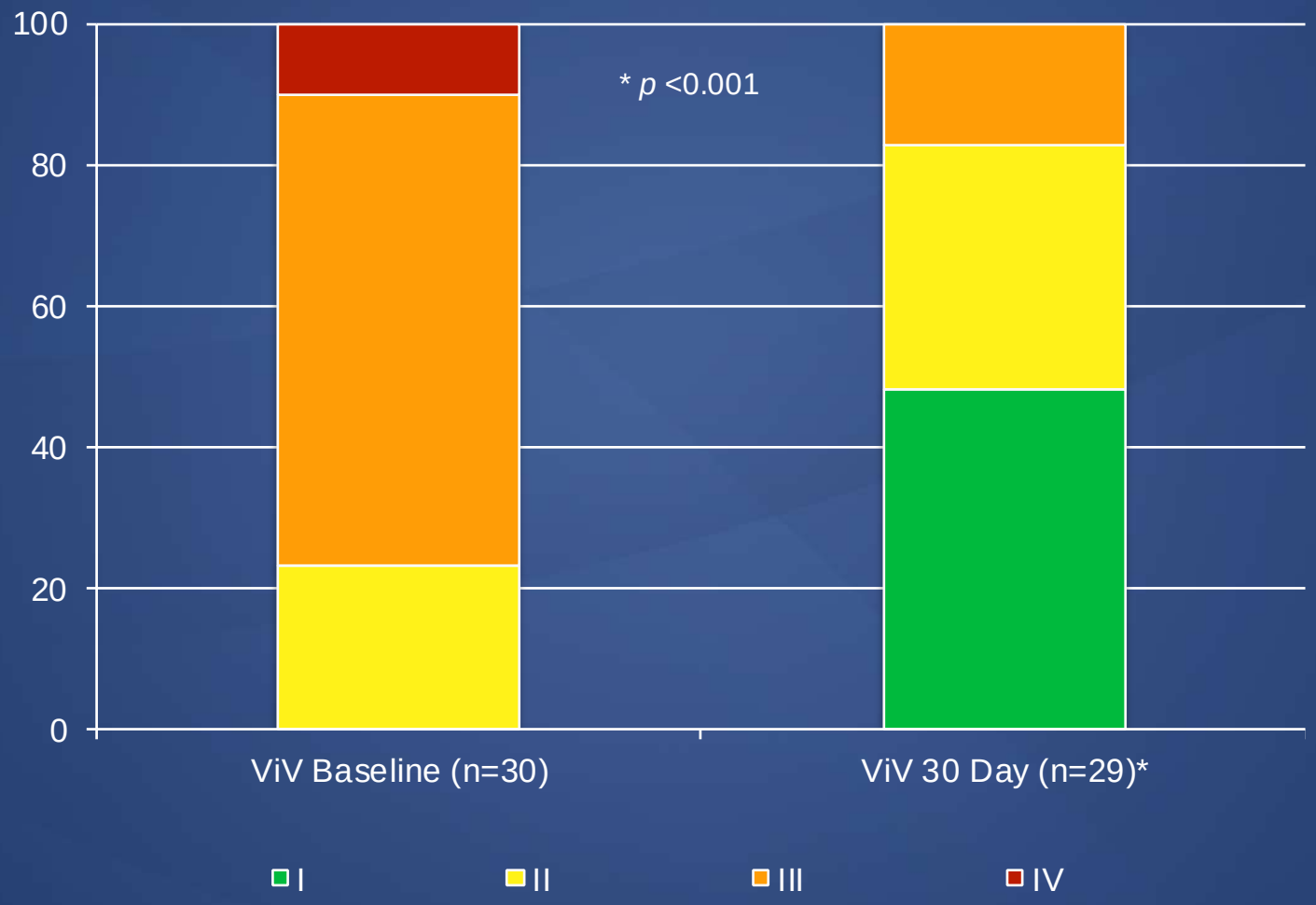
MITRAL Trial

NYHA Class at 30 days



1 patient died on POD #29

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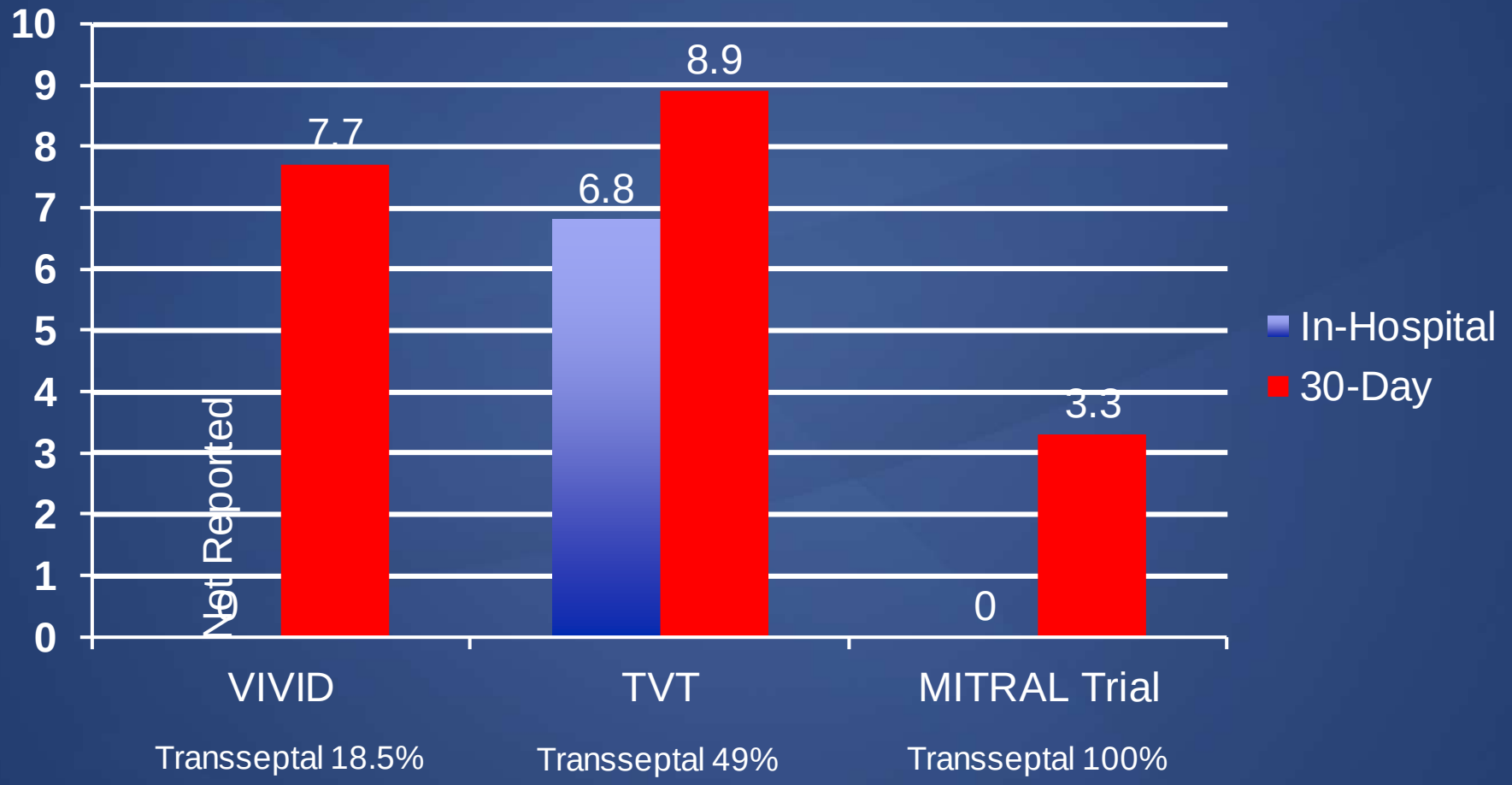
Mitral ViV All-cause Mortality



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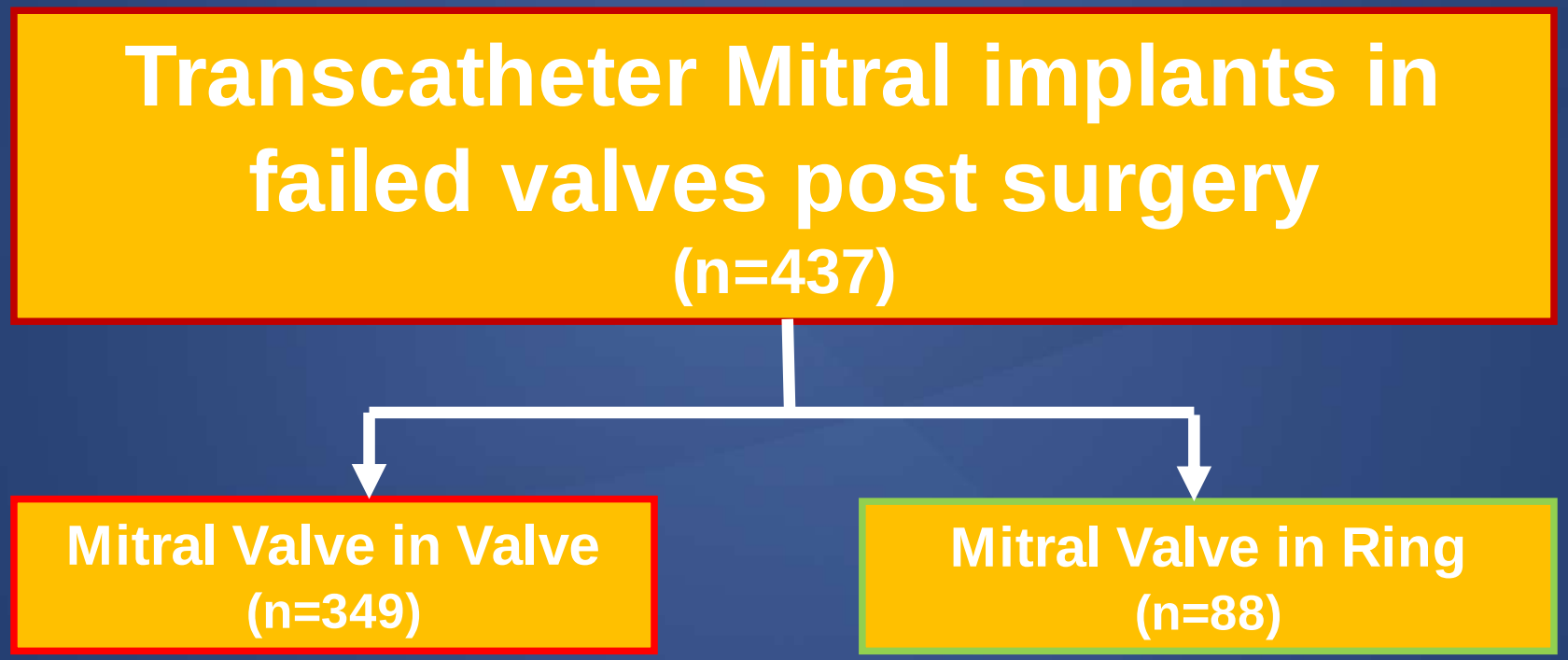
VIVID Registry

Median follow up : 408 days



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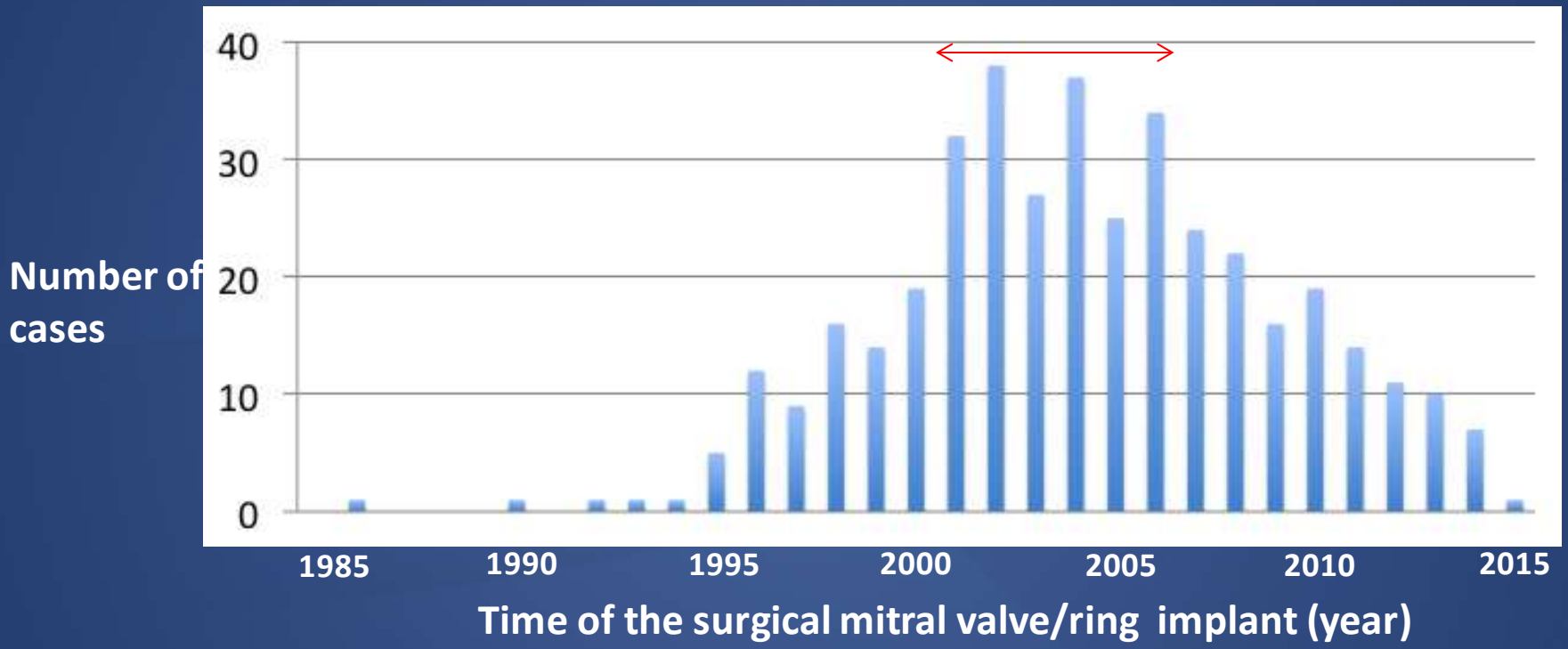
Index Cardia Surgery

•Median 9 years since last cardiac surgery (IQR 5-12).



- 1-5 previous cardiac surgeries per patient.
- 71% of patients had 1 previous cardiac surgery.

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Surgical Mitral Bioprosthesis

Type	n	%	Size	n	%
Edwards Pericardial / Porcine	171	52.9	23 mm	2	0.6
Medtronic Mosaic	67	19.2	25 mm	42	12
Medtronic Hancock	49	14	27mm	128	36.7
St Jude Epic	26	7.4	29 mm	110	31.5
St Jude Biocor	14	4	31 mm	48	13.8
Braile Porcine Biomedica	4	1.1	33 mm	9	2.6
Other / Unknown	18	5.2	Other / unknown	10	2.9

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Surgical Mitral Ring

Type	n	%	Size	n	%
Edwards Physio I / II	50	56.8	26 mm	11	12.5
Medtornic Duran	7	8	28 mm	29	33
St Jude Seguin	6	6.8	30 mm	14	15.9
Edwards Classic	5	5.7	32 mm	9	10.2
Medtronic other	4	4.5	34 mm	6	6.8
Sorin Carbomedics	2	2.2	36 mm	2	2.3
Other / Unknown	14	15.9	Other / unknown	17	19.3

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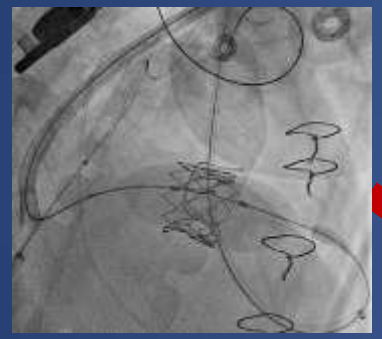
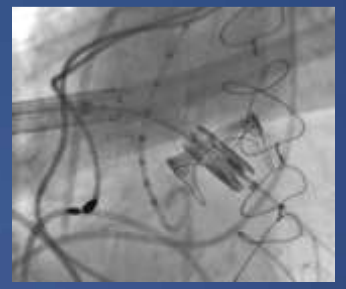
VIVID Registry

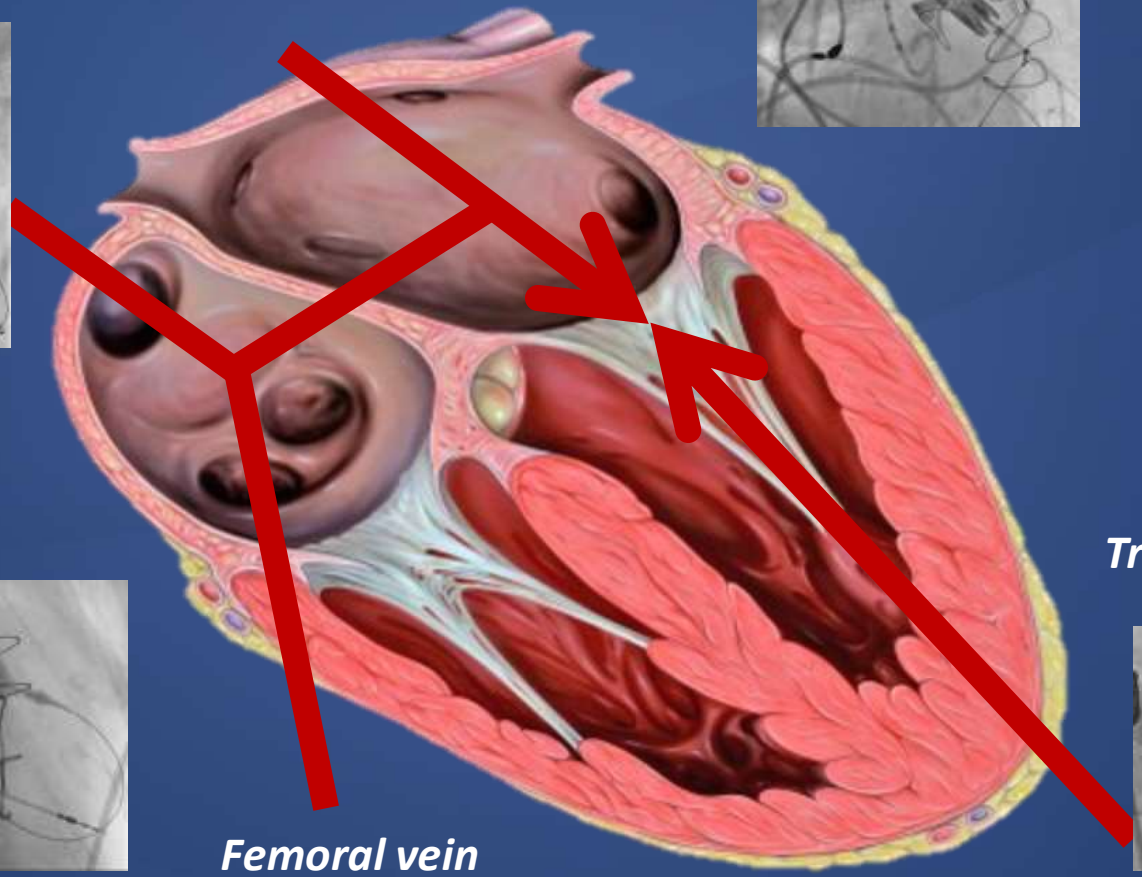
Access during Mitral ViV procedure

Jugular Vein

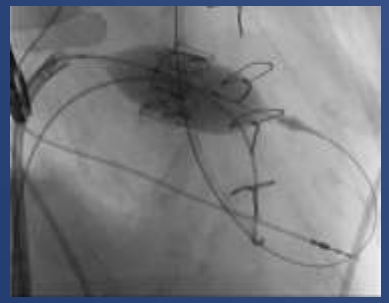


Direct left atrium





Total trans-septal



Femoral vein

Transapical

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VIVID Registry

Mitral ViV Procedural Outcomes

	Total n=437	Mitral Valve-in-Valve n=349	Mitral Valve-in-Ring n=88	P Value
30-day death	8.5%	7.7%	11.4%	0.15
30-day cardiovascular death	6.9%	6%	10.2%	0.62
Major stroke	2.5%	2.9%	1.1%	0.33
Acute kidney injury (VARC II/III)	14.4%	10.6%	29.5%	<0.001

Ran Kornowski, TVT 2018

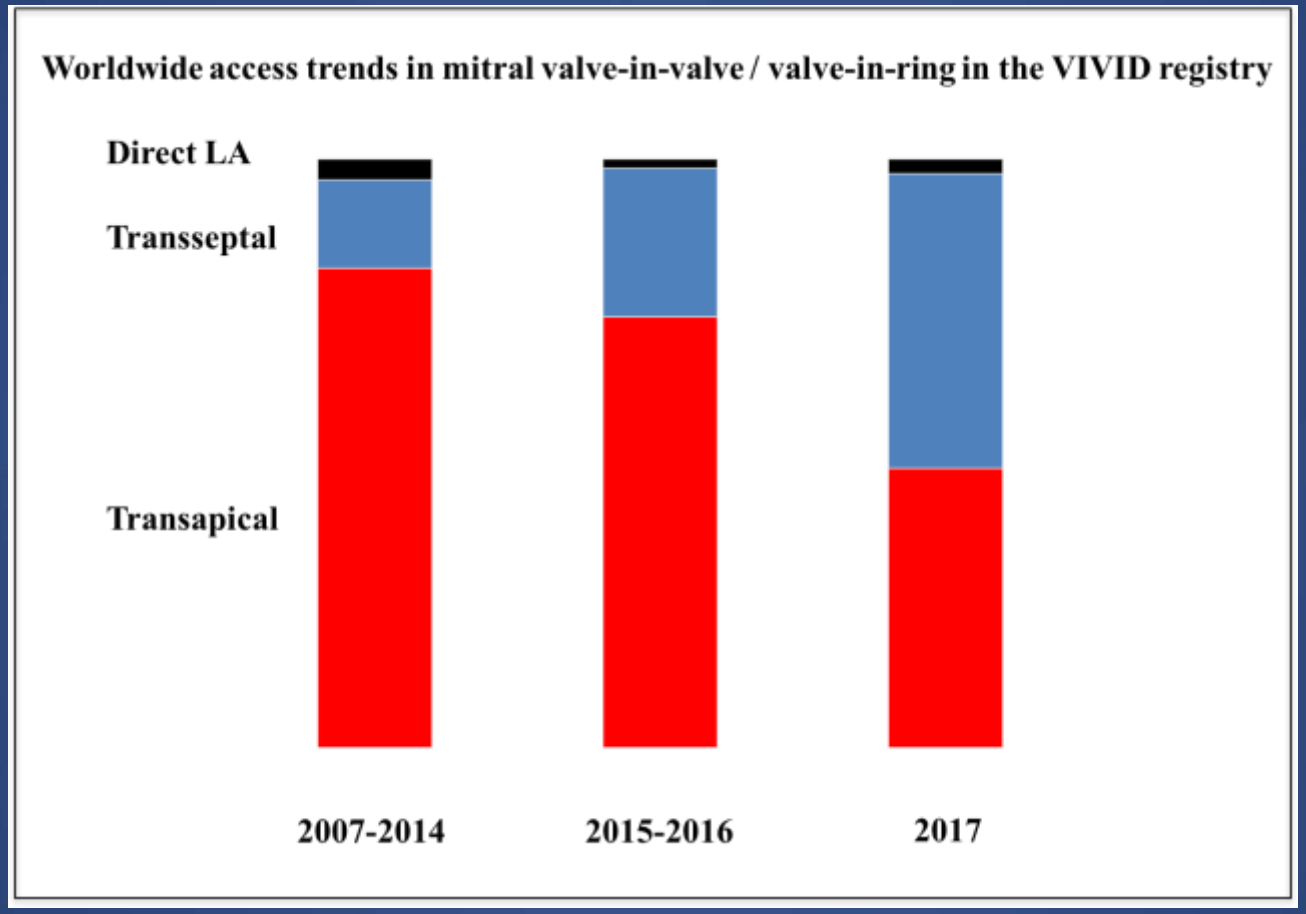
VIVID Registry

Composite (30d event-free) End point*

*Composite end point included 30-day survival free from significant MR (moderate or more) or clinically-evident LVOT obstruction. The composite of adverse events occurred in 39 patients undergoing valve-in-valve and 25 patients that underwent valve-in-ring.

Ran Kornowski, TVT 2018

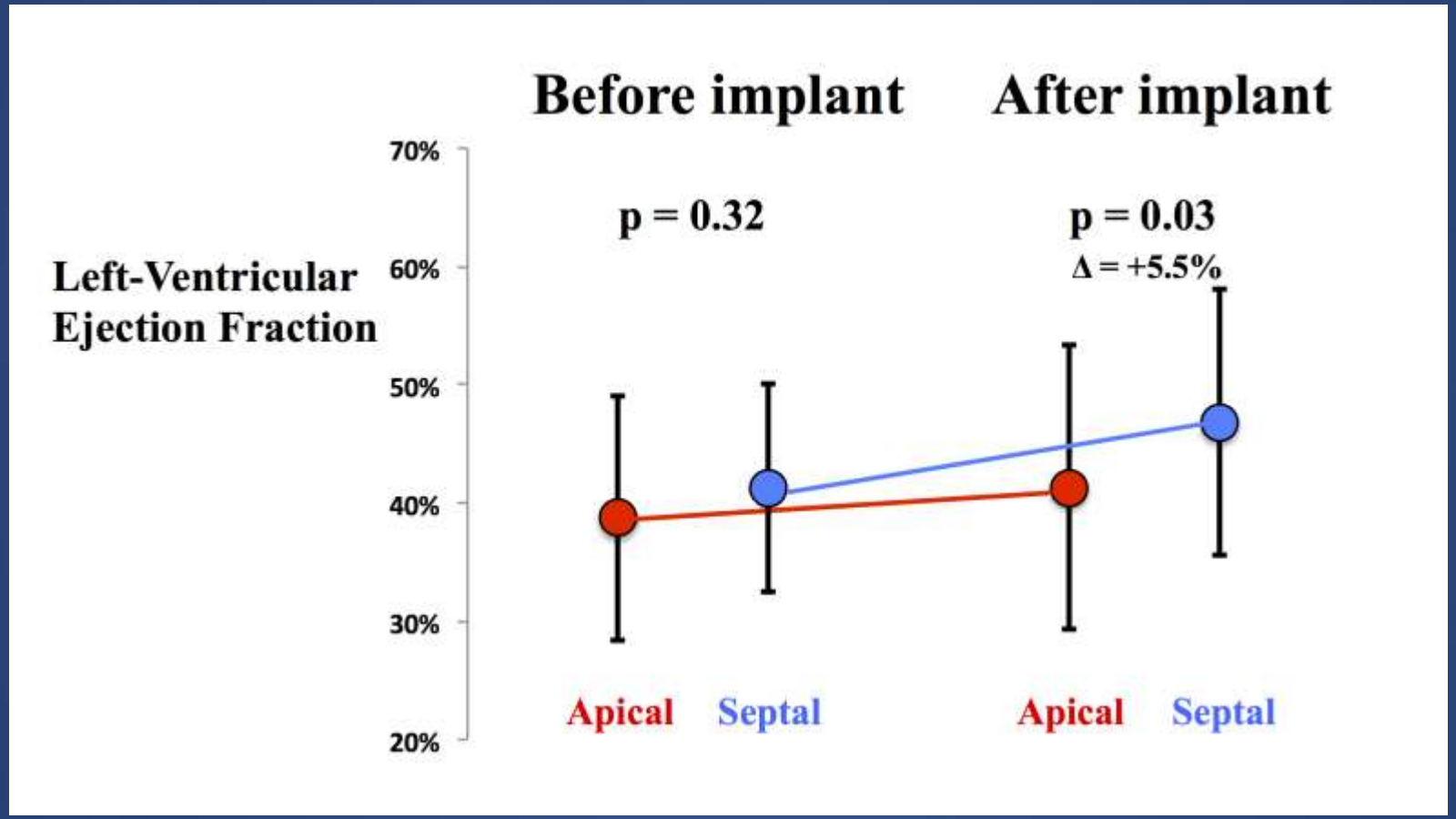
VIVID Registry



Transseptal SAPIEN 3 MViV is currently the most common approach

Ran Kornowski, TVT 2018

LV function according to access route



Dvir D. JACC CV Interv 2016.

Transcatheter MVI: 7-year experience
Procedural findings and outcomes

Table 2 Procedural findings and outcomes

	Entire cohort (*n* = 91)	Valve-in-valve (*n* = 34)	Valve-in-ring (*n* = 30)	Valve-in-MAC (n = 27)	*P*-value
Procedural findings					
Approach					
Transeptal	84 (92.3)	32 (94.1)	30 (100)	22 (81.5)	0.027
Transapical/Hybrid surgery	7 (7.7)	2 (5.9)	0	5 (18.5)	
Prosthesis type					
SAPIEN XT	37 (40.7)	15 (44.1)	17 (58.6)	5 (18.5)	0.008
SAPIEN 3	53 (58.2)	19 (55.9)	12 (41.4)	22 (81.5)[a,b]	
Prosthesis size (mm)					
23	6 (6.6)	2 (5.9)	4 (13.8)	0	<0.001
26	49 (53.8)	16 (47.1)	22 (75.9)[c]	11 (40.7)[b]	
29	35 (38.5)	16 (47.1)	3 (10.3)[c]	16 (59.3)	
Post-dilatation	17 (18.7)	2 (5.9)	10 (35.7)[c]	5 (18.5)	0.009
Need for a second valve	13 (14.3)	1 (2.9)	5 (16.7)	6 (22.2)[a]	0.043
Procedural outcomes					
Technical success	77 (84.6)	32 (94.1)	24 (80.0)	21 (77.7)	0.196
Death	1 (1.1)	1 (2.9)	0	0	0.999
Conversion to surgery	2 (2.2)	0	2 (6.7)	0	0.192
Tamponade	0	—	—	—	—
Haemodynamically significant LVOT obstruction (gradient ≥50 mmHg)	3 (3.3)	1 (2.9)	0	2 (7.4)	0.388
Prosthesis embolization	2 (2.2)	1 (2.9)	1 (3.4)	0	0.999

LVOT, left ventricular outflow tract.
[a]$P < 0.05$ vs. valve-in-valve.
[b]$P < 0.05$ vs. valve-in-ring.
[c]$P < 0.05$ vs. valve-in-valve.

Marina Urena. EHJ 2018.

Transcatheter MVI: 7-year experience
30 day outcomes

	Entire cohort ($n = 91$)	Valve-in-valve ($n = 34$)	Valve-in-ring ($n = 30$)	Valve-in-MAC ($n = 27$)	*P*-value
Death	7 (7.7)	2 (5.9)	2 (6.7)	3 (11.1)	0.788
Surgical mitral valve replacement	4 (4.4)	0	4 (13.3)	0	0.017
Stroke	4 (4.4)	2 (5.9)	0	2 (7.4)	0.455
Major	2 (2.2)	0	0	2 (7.4)	0.086
Minor	2 (2.2)	2 (5.9)	0	0	0.329
Life-threatening or fatal bleeding	4 (4.4)	2 (5.9)	1 (3.3)	1 (3.7)	0.999
Major vascular complications	6 (6.7)	2 (5.9)	2 (6.7)	2 (7.4)	0.999
LVOT obstruction (ΔP increase >30 mmHg)	8 (8.8)	2 (5.9)	4 (13.3)	2 (7.4)	0.648
Late valve embolization	0	—	—	—	—
Slight late displacement of the THV	3 (3.3)	0	0	3 (11.1)	0.023
THV thrombosis	8 (8.8)	3 (8.8)	2 (6.7)	3 (11.1)	0.900

LVOT, left ventricular outflow tract; MR, mitral regurgitation; THV, transcatheter heart valve; TMVI, transcatheter mitral valve implantation; ΔP, basal maximal gradient.

Marina Urena. EHJ 2018.

Transcatheter MVI: 7-year experience

Cumulative Clinical Outcomes

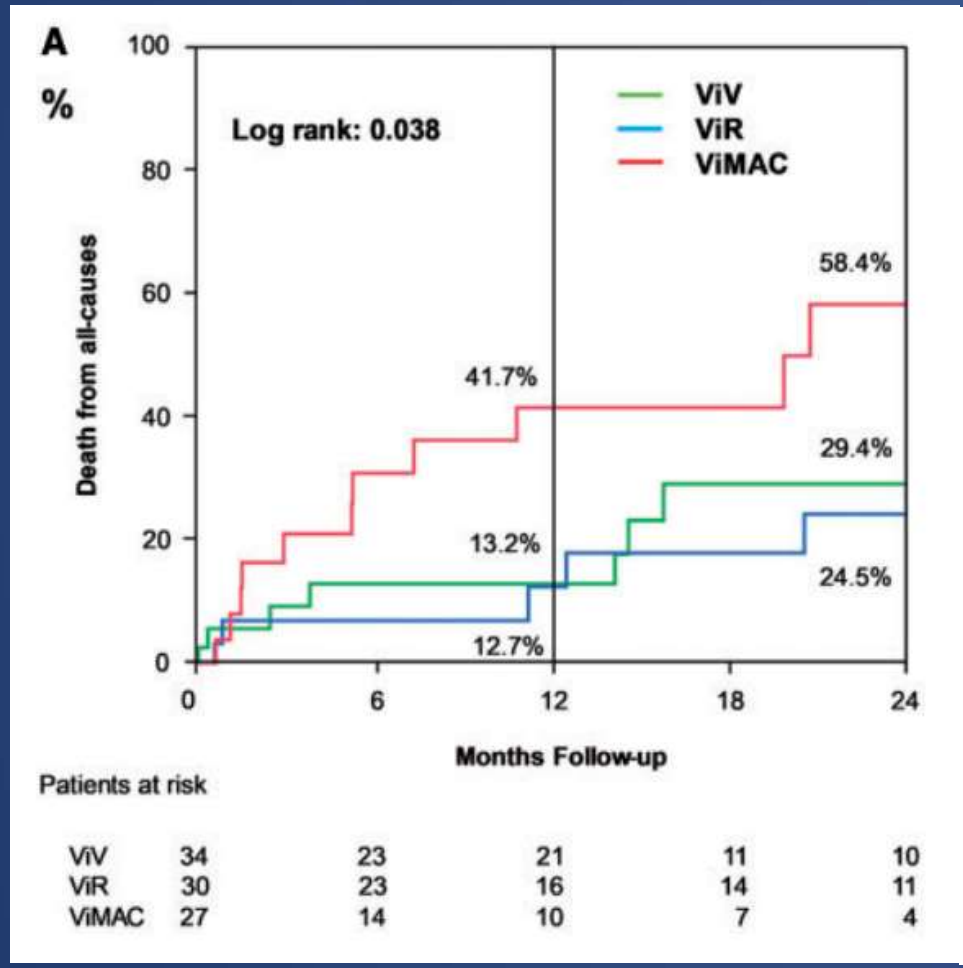
	Entire cohort ($n = 91$)	Valve-in-valve ($n = 34$)	Valve-in-ring ($n = 30$)	Valve-in-MAC ($n = 27$)	*P*-value
Death					
n (%)	30 (33.0)	8 (23.5)	10 (33.3)	12 (44.4)	
HR (95% CI)		1.0	0.82 (0.29–2.31)	2.39 (1.01–5.86)[a]	0.046
Cardiovascular death					
n (%)	24 (26.4)	5 (14.7)	10 (33.3)	9 (33.3)	
HR (95% CI)		1.0	1.30 (0.40–4.16)	2.80 (0.94–8.46)	0.125
Death or surgical valve replacement					
n (%)	36 (39.6)	8 (23.5)	16 (53.3)	12 (44.4)	
HR (95% CI)		1.0	1.58 (0.65–3.85)	2.34 (0.96–5.75)	0.175
Surgical mitral valve replacement					
n (%)	7 (7.7)	0	7 (23.3)	0	
HR (95% CI)		1.0	—	—	—

CI, confidence interval, HR, hazard ratio.
[a]$P < 0.05$ vs. valve-in-ring.

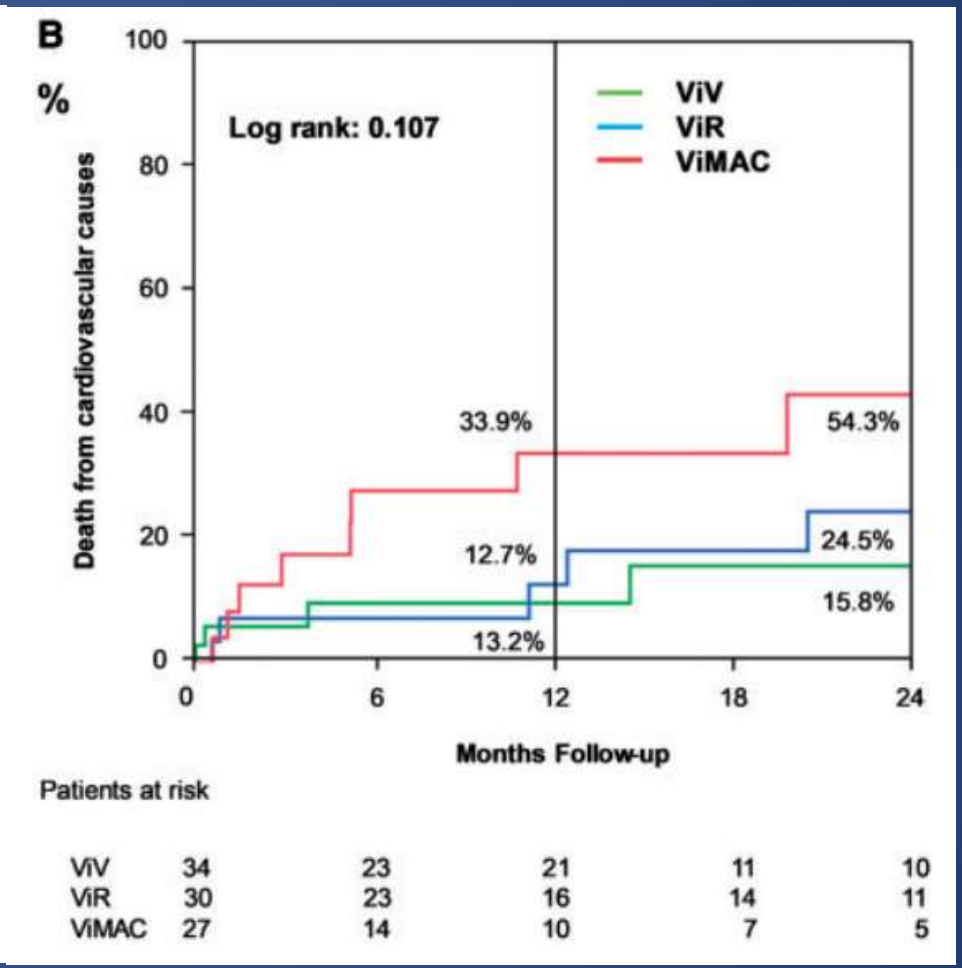
Marina Urena. EHJ 2018.

Transcatheter MVI: 7-year experience

All cause death



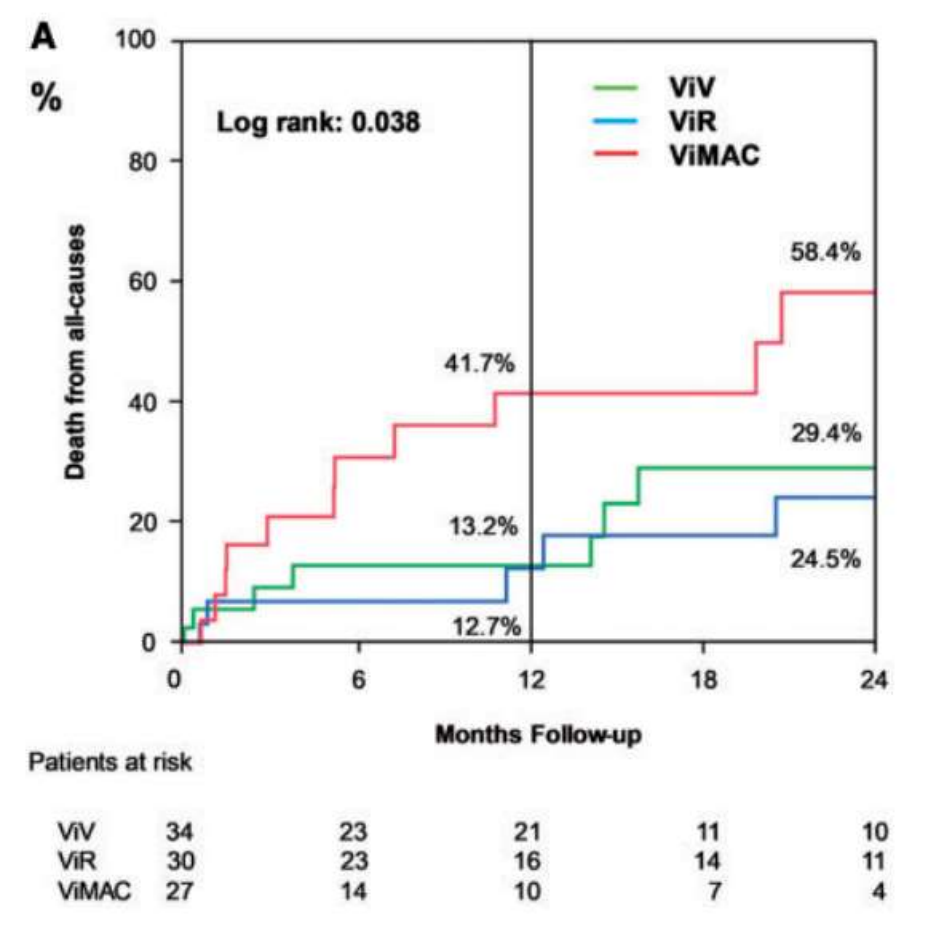
CV death



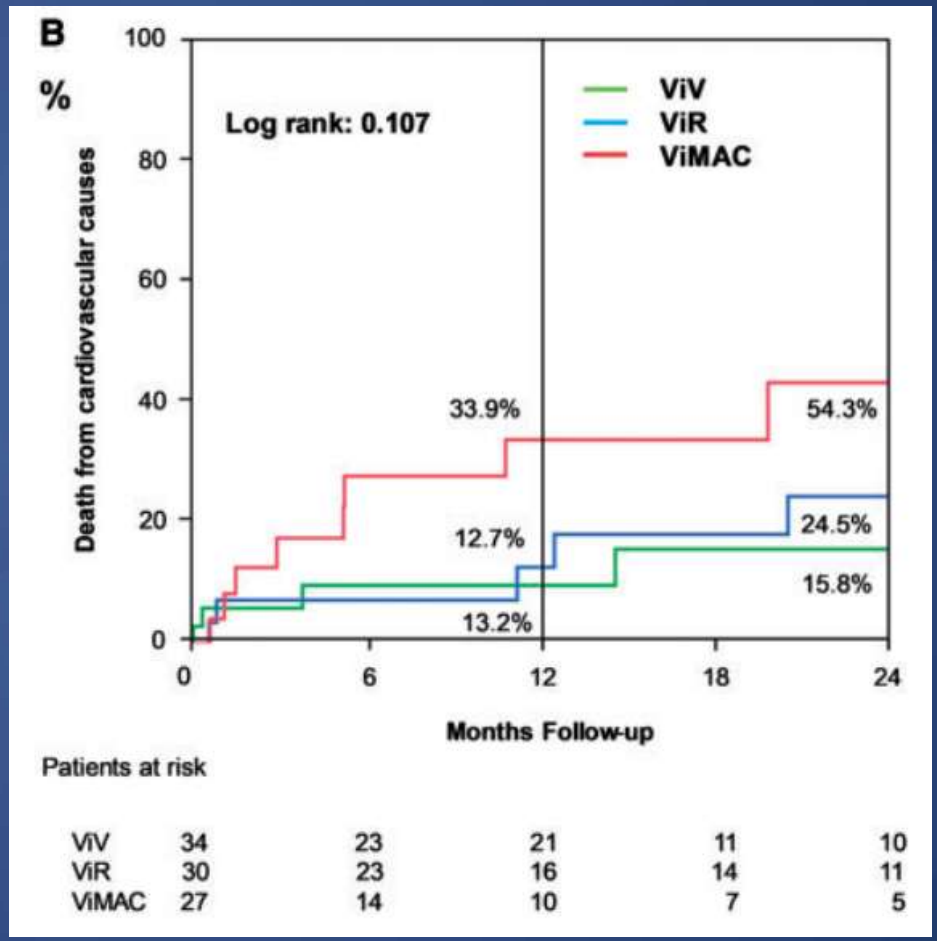
Marina Urena. EHJ 2018.

Transcatheter MVI: 7-year experience

All cause death



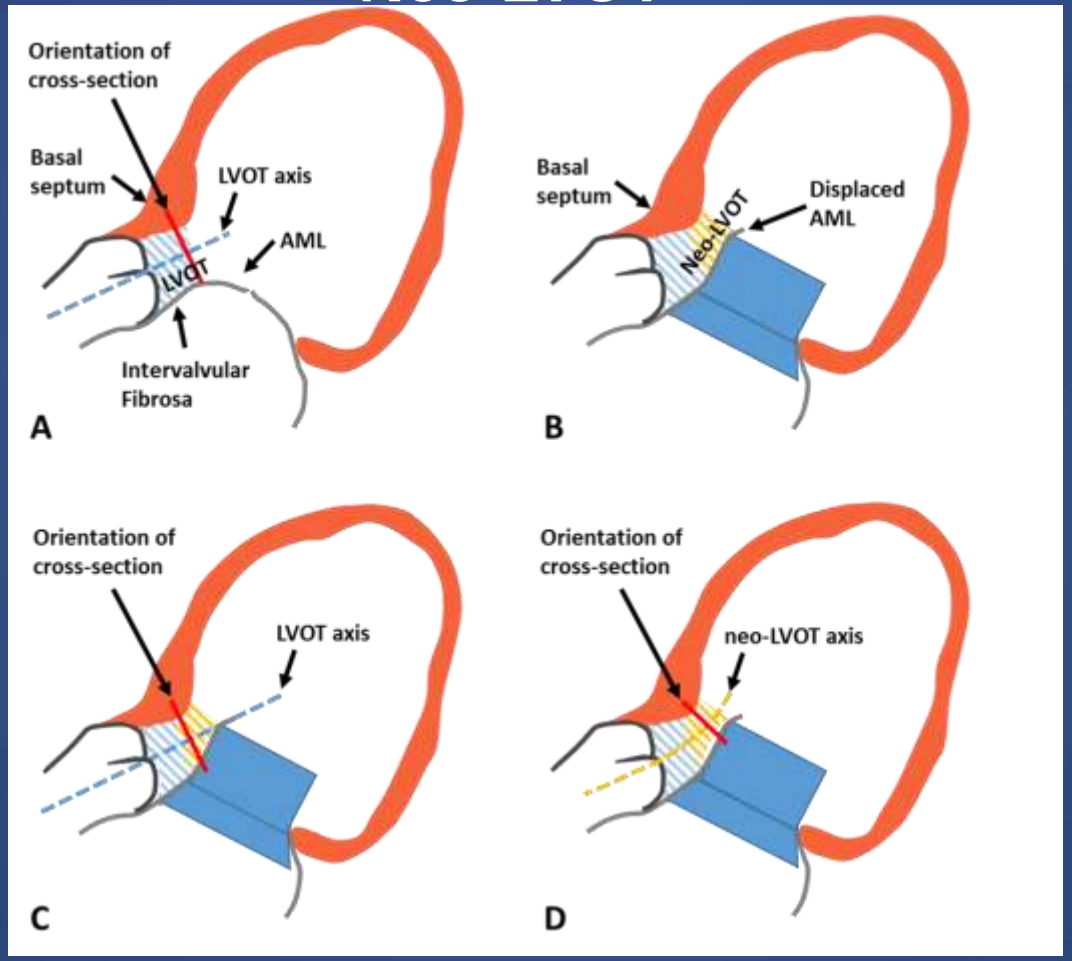
CV death



Marina Urena. EHJ 2018.

Prediction of LVOT obstruction

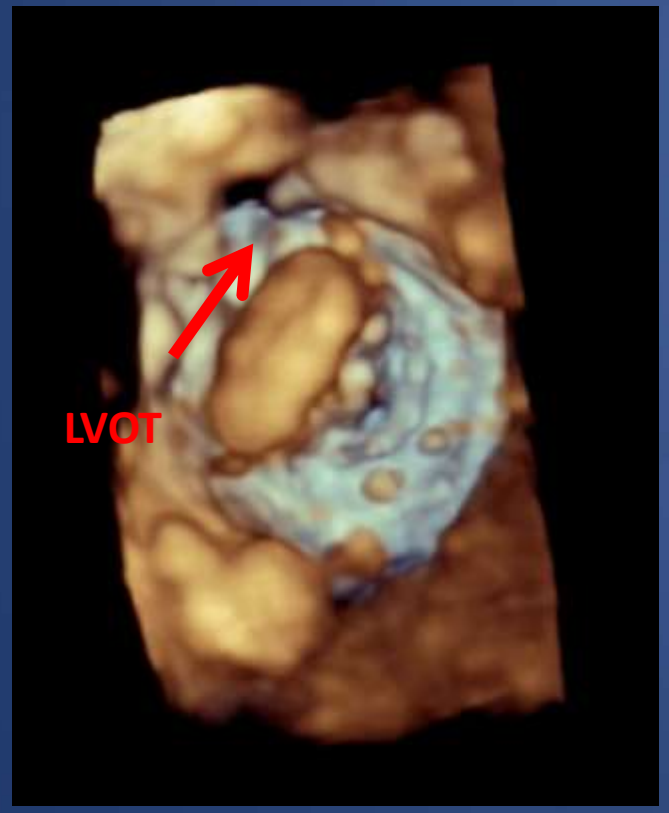
Neo-LVOT

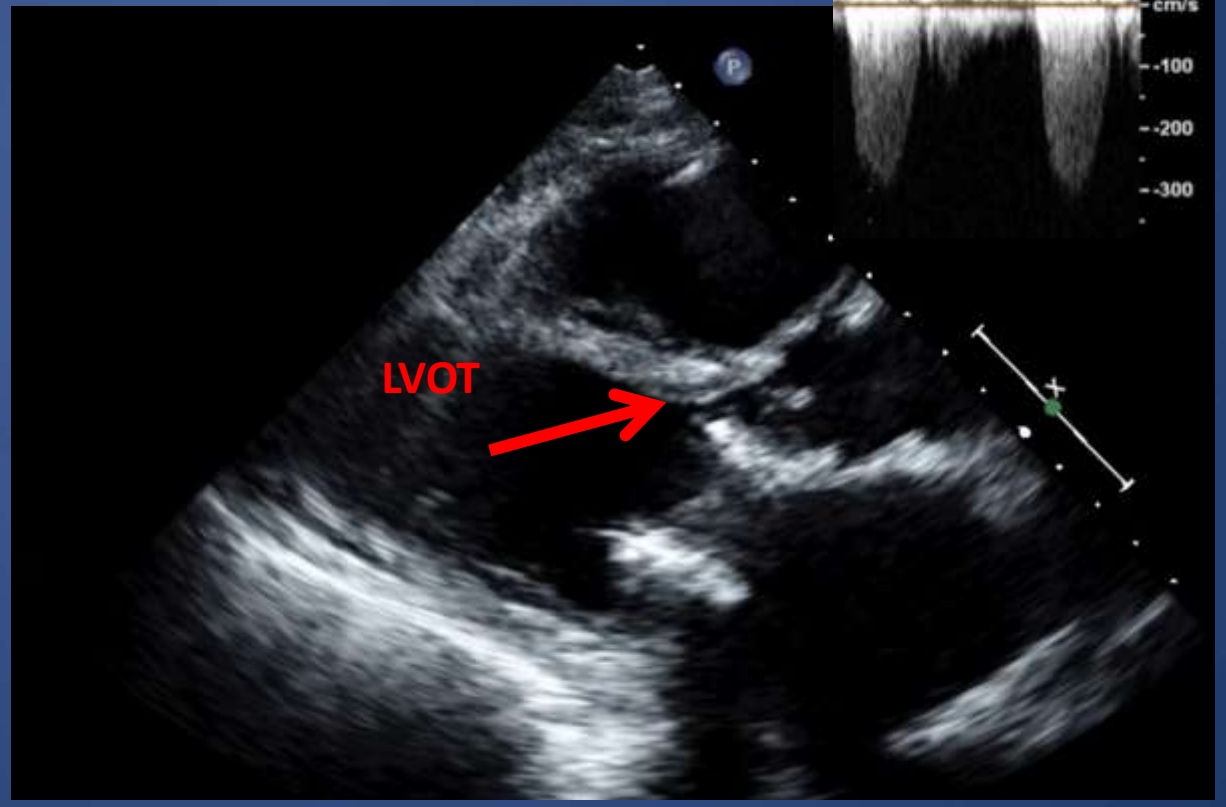


Blanke P. JACC CV imaging 2016.

High risk for LVOT obstruction

- 3.7% in the studied population.
- More common after Valve-in-Ring (8% vs. 2.6% in Valve-in-Valve , p=0.03).





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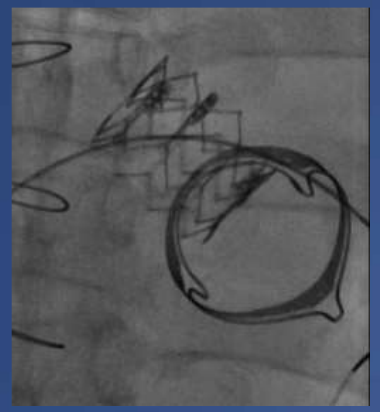
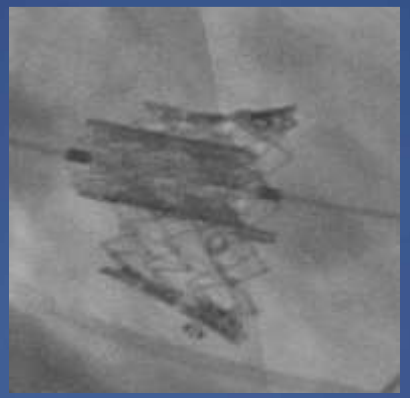
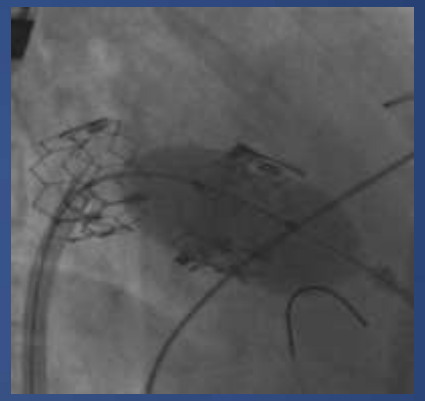
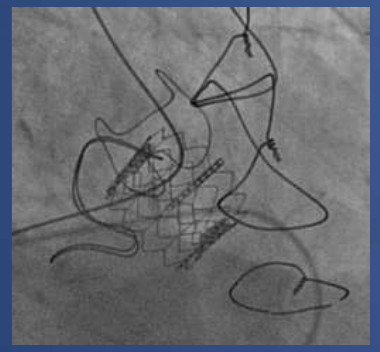
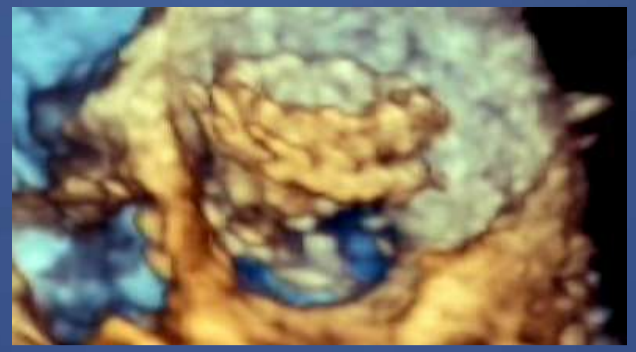
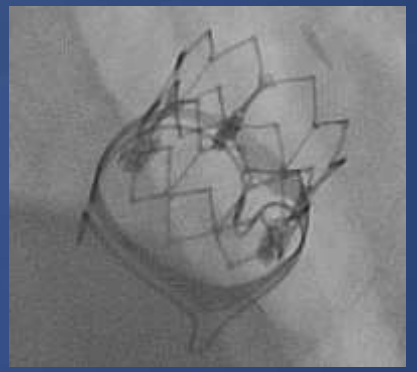
Mal-positioning

- 29 mal-positioning events (6.6%).
- 20 Implantation of another transcatheter device (4.6%).

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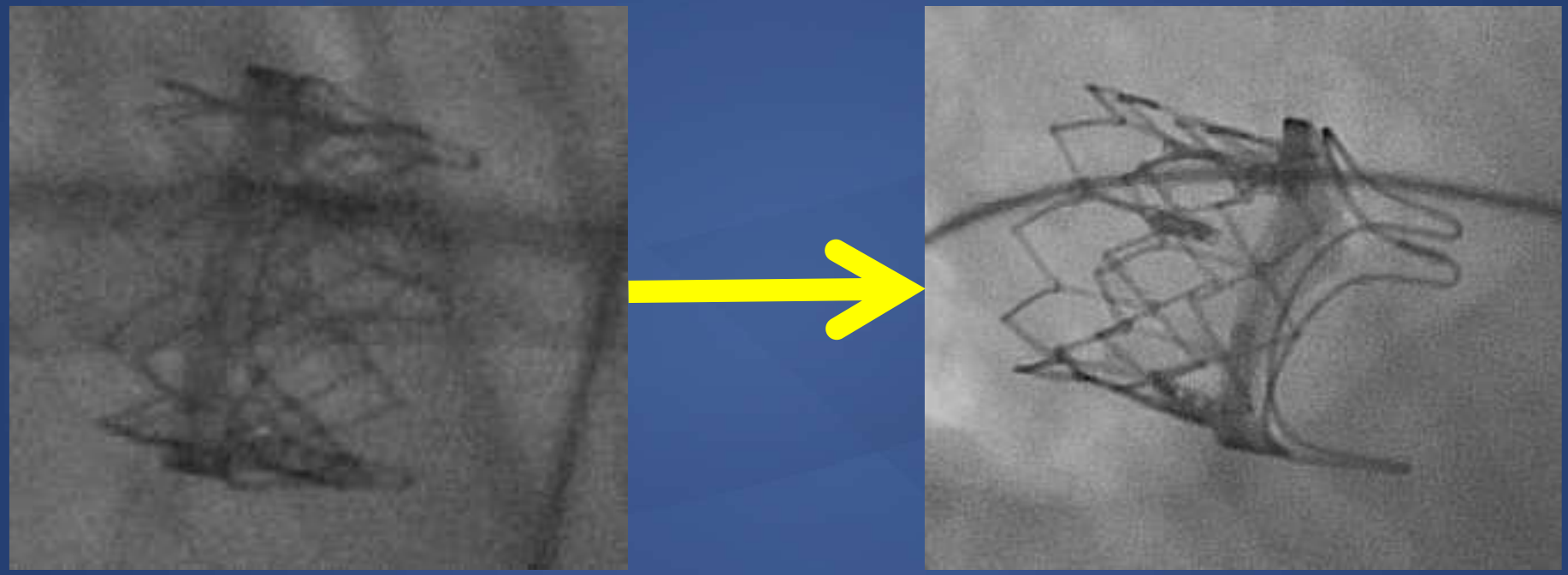
Delayed Mal-positioning



Mitral Valve-in-Valve

After 2 months

Delayed malpositioning (>1 week) in 1.1%.

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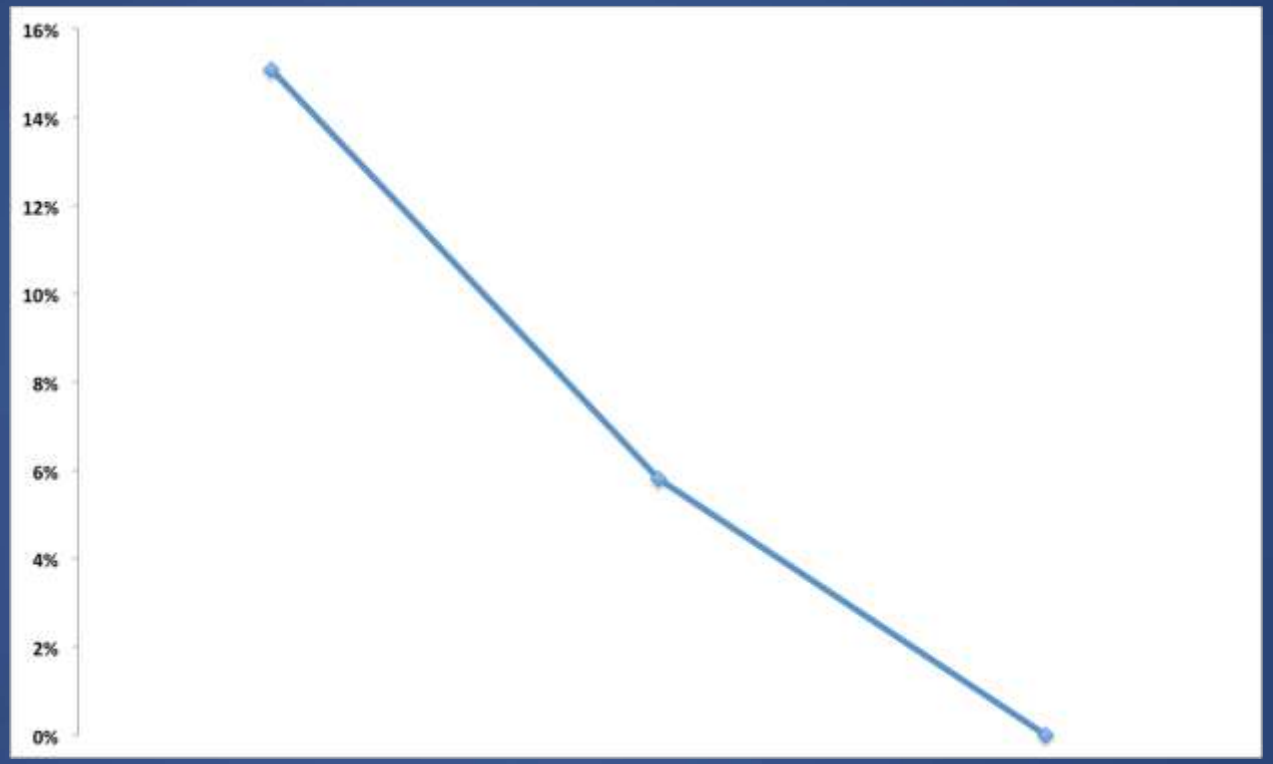
Residual stenosis

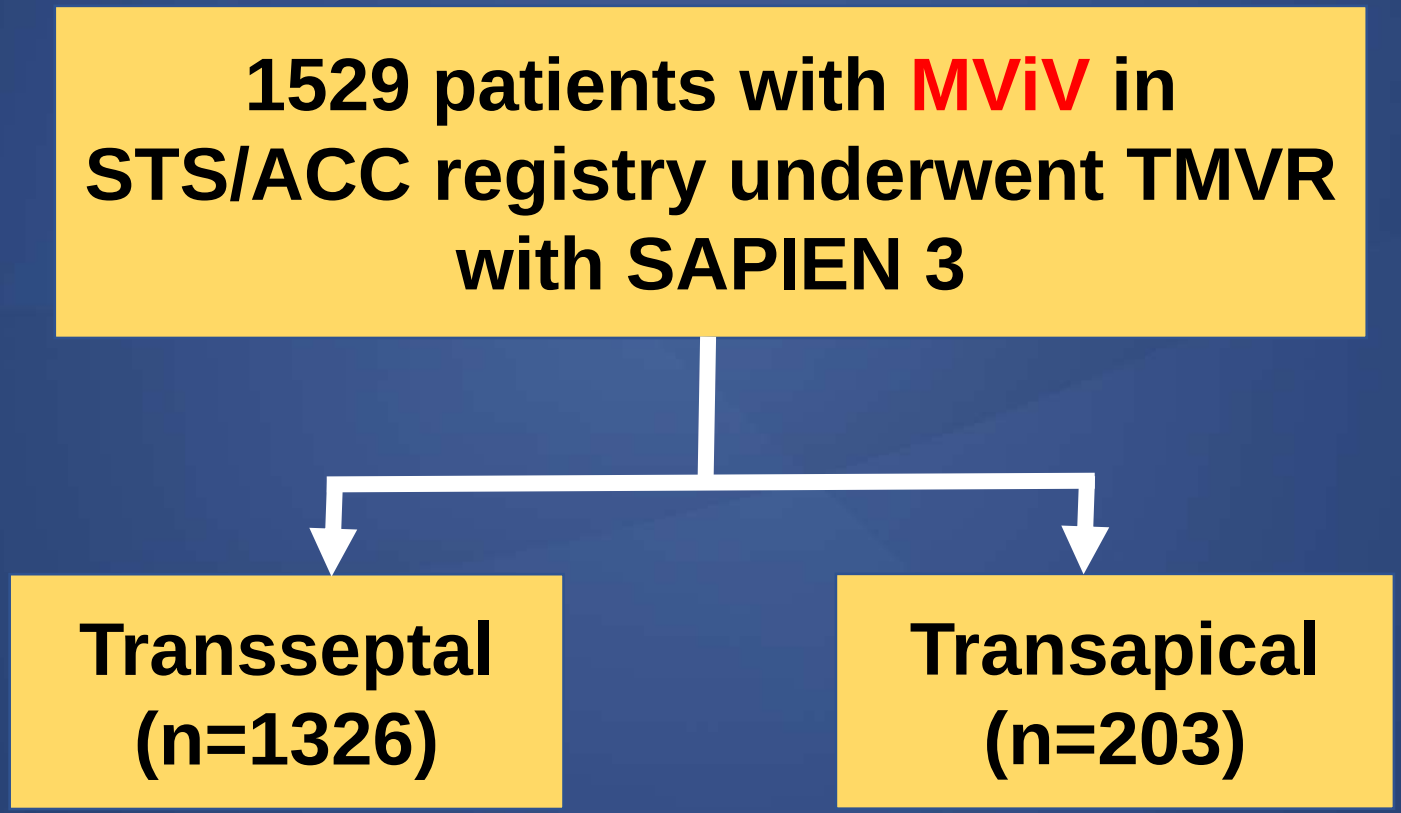
Elevated post procedural gradients (mean>=10mmHg)



Small valves	Intermediate valves	Large valves
ID<=24	ID>24 & <=27	ID>27

Ran Kornowski, TVT 2018

One-Year Outcomes of Mitral VIV using SAPIEN 3



Brian Whisenant, 2020 JAMA

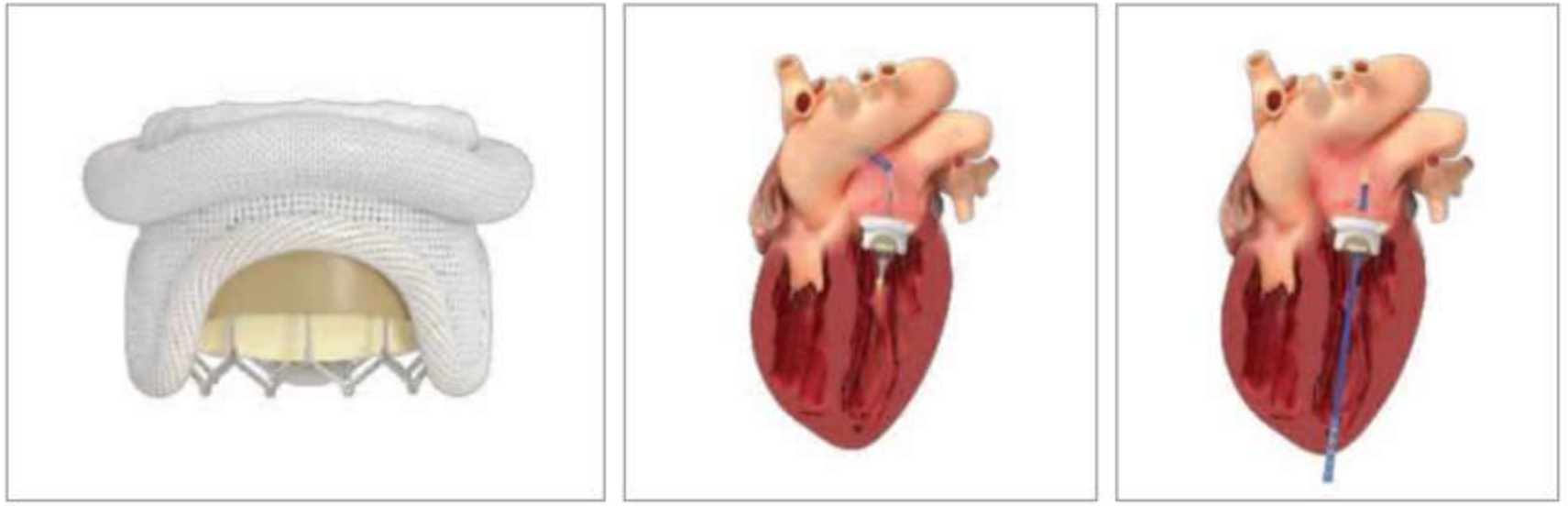
One-Year Outcomes of Mitral VIV using SAPIEN 3

Figure 1. SAPIEN 3 Transcatheter Heart Valve , Transseptal, and Transapical Access Approaches

A SAPIEN 3 within stented bioprosthetic valve

B Transseptal mitral valve-in-valve

C Transapical mitral valve-in-valve



Brian Whisenant, 2020 JAMA

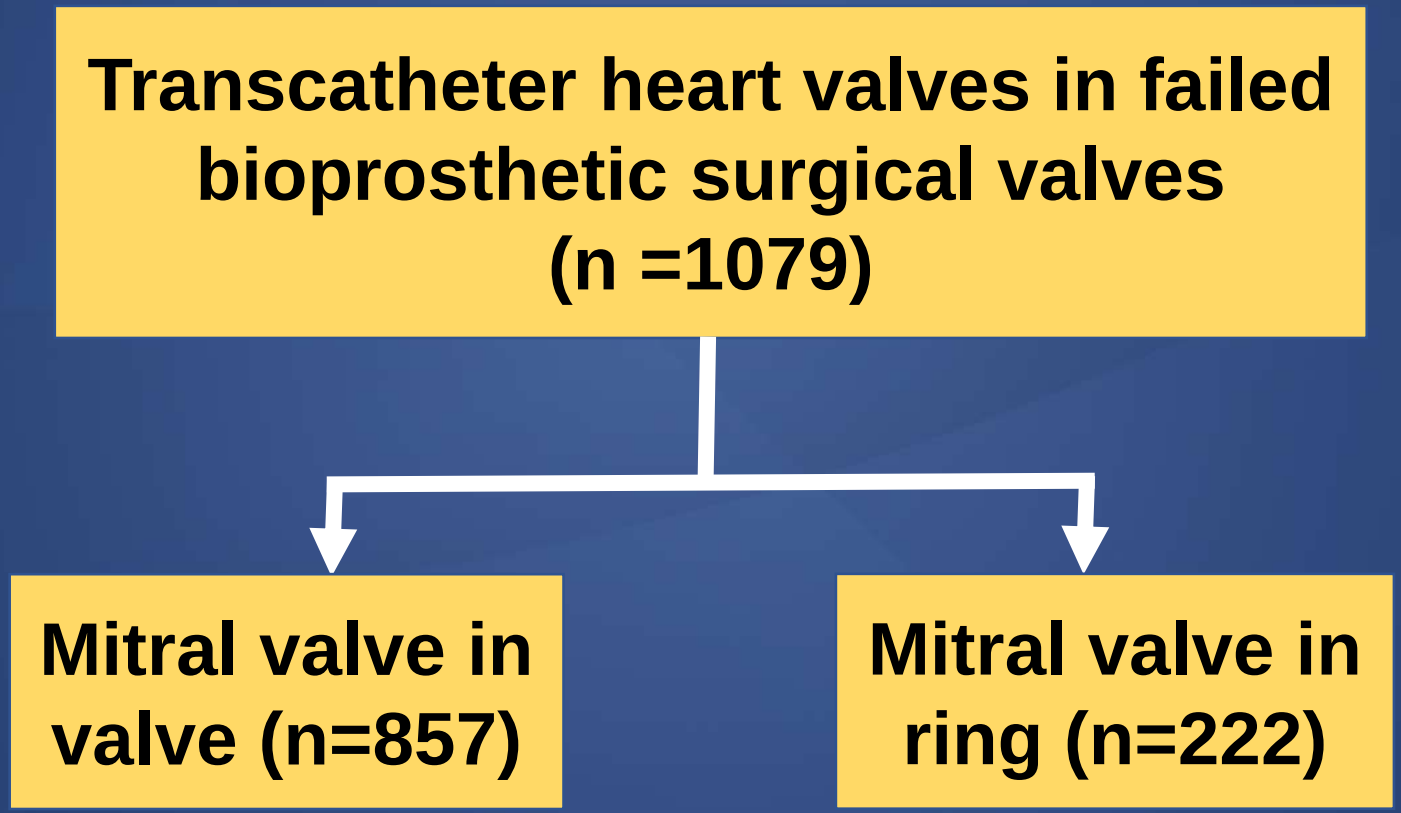
One-Year Outcomes of Mitral VIV using APIEN 3

Outcome	No./total No. (%) of patients			P value
	Transseptal (n = 1326)	Transapical (n = 203)	Combined (N = 1529)	
1-y Outcomes				
All-cause mortality	138 (15.8)	37 (21.7)	175 (16.7)	.03
All-cause mortality No. at risk	438	97	535	NA
Cardiovascular death	36 (3.7)	11 (5.7)	47 (3.9)	.07
Stroke	27 (3.3)	5 (3.5)	32 (3.3)	.95
Mitral valve reintervention	8 (0.8)	1 (0.5)	9 (0.8)	.78
New dialysis requirement	19 (1.6)	6 (3.1)	25 (1.8)	.13
New pacemaker	21 (2.0)	5 (2.8)	26 (2.1)	.44
Device thrombosis	4 (0.3)	2 (1.2)	6 (0.5)	.17
LV ejection fraction, mean (SD), %	53.3 (11.52)	52.8 (13.11)	53.2 (11.76)	.77
Mean MVG, mean (SD), mm Hg	7.0 (2.94)	7.0 (2.61)	7.0 (2.89)	.99
1-y KCCQ Improvement, mean (SD)	40.2 (27.26)	35.3 (26.37)	39.4 (27.14)	.27
1-y NYHA class				
I	143/290 (49.3)	30/62 (48.4)	173/352 (49.1)	.89
II	119/290 (41.0)	26/62 (41.9)	145/352 (41.2)	.90
III	23/290 (7.9)	5/62 (8.1)	28/352 (8.0)	>.99
IV	5/290 (1.7)	1/62 (1.6)	6/352 (1.7)	>.99

Brian Whisenant, 2020 JAMA

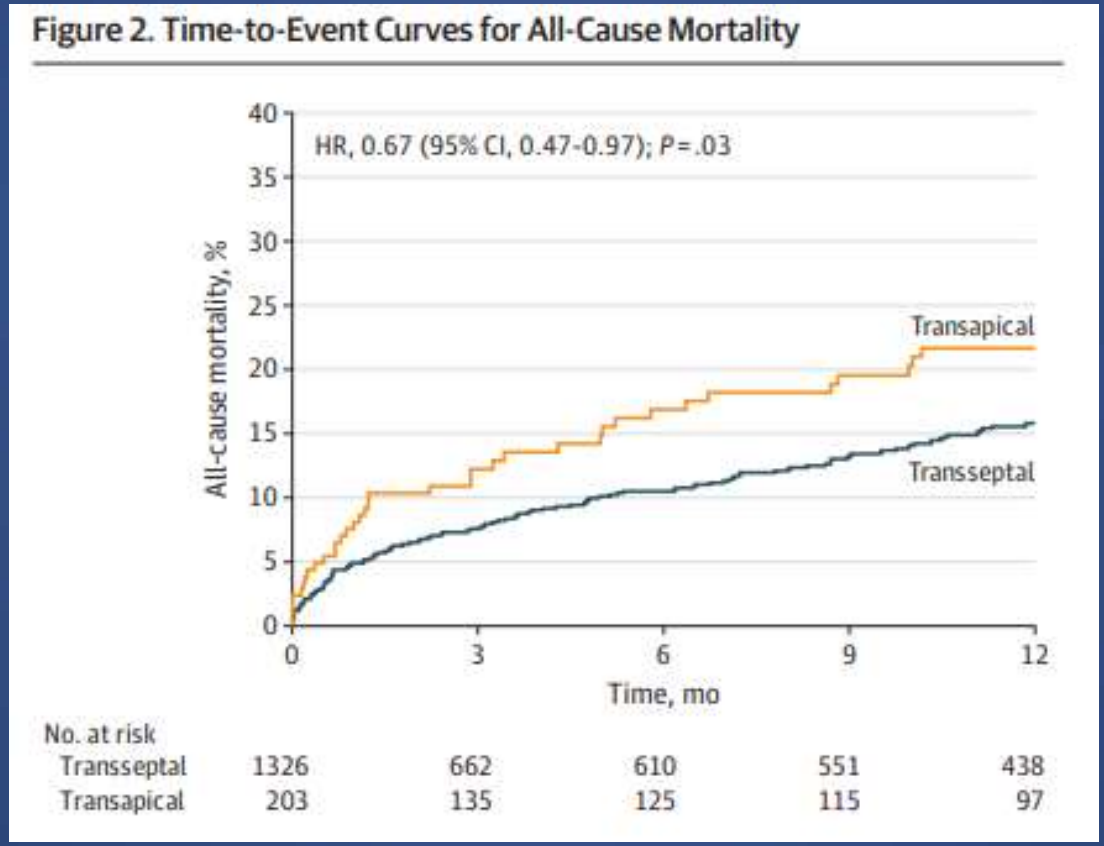
Comprehensive midterm evaluation of VIVID Registry

Median follow up : 492 days



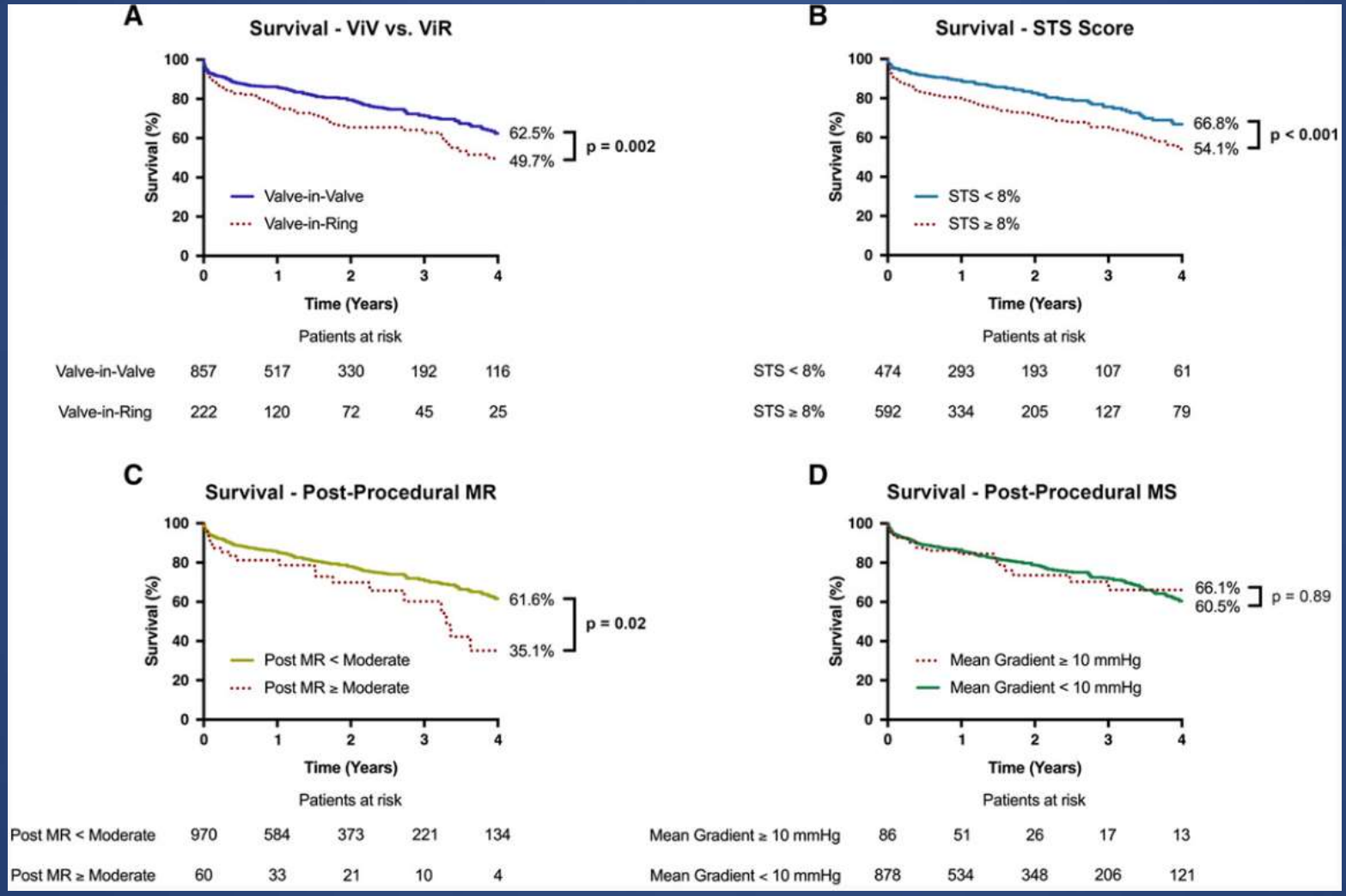
Matheus Simonato, 2021 circulation

One-Year Outcomes of Mitral VIV using SAPIEN 3



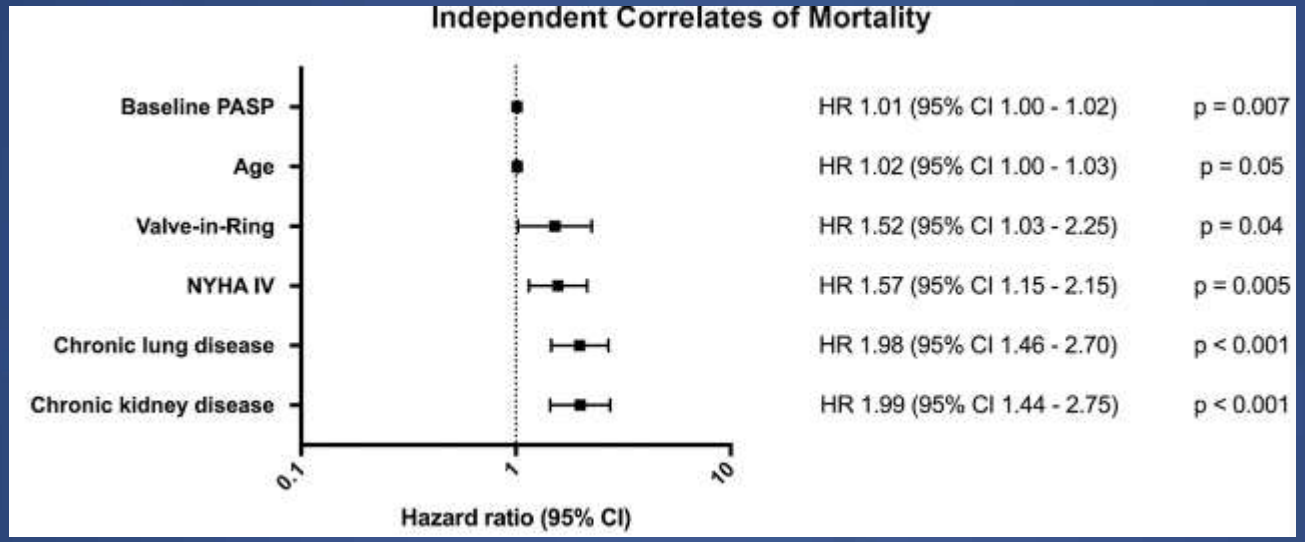
Brian Whisenant, 2020 JAMA

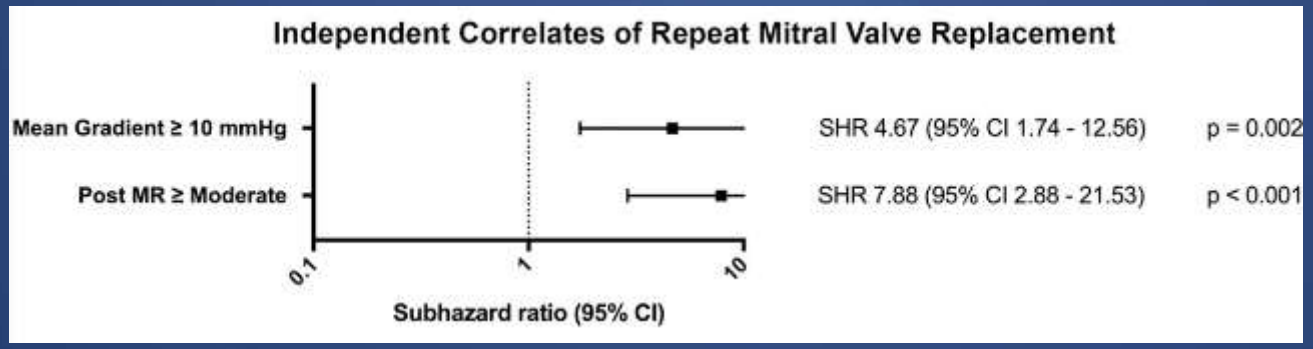
Comprehensive midterm evaluation of VIVID Registry



Matheus Simonato, 2021 circulation

Comprehensive midterm evaluation of VIVID Registry





Matheus Simonato, 2021 circulation

MITRAL trial Valve-in-Valve Arm 1-Year Outcomes

Patient Flow

38 patients presented in case review call* → 8 patients excluded:
3= Right Ventricular Dysfunction
2= Became unstable requiring pressors
1= No central MR, mostly PVL
1= LV EF barely 20%, considered cohort "C"
1= Risk of LVOTO

↓

30 patients enrolled

↓

1 Non-Cardiovascular Death on day 29

↓

30-Day follow-up in 29 (100%)

↓

No deaths after 30 days

↓

1 year follow-up in 29/29 (100%)

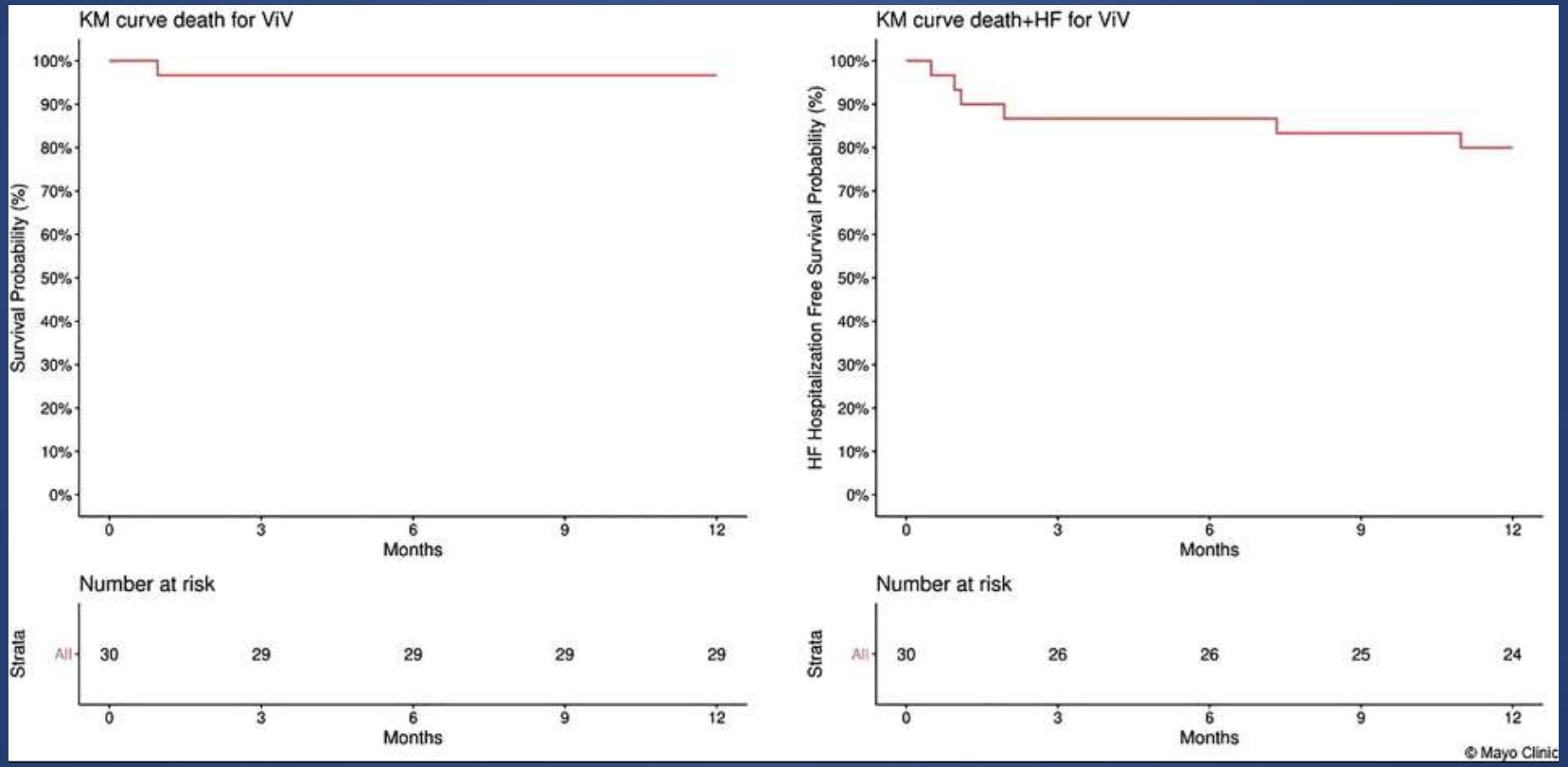
Valve Type	n
Edwards perimount Family (perimount Magna Ease, Baxter)	16
Medtronic Mosaic	6
St. Jude Biocor/Epic	5
Edwards CE Standard	3

Failure mode	n(%)
Regurgitation	18 (60%)
Stenosis	8 (26.7%)
Both	4 (13.3%)

*All patients presented at case review call
All CT scans reviewed by Core Lab prior to presentation

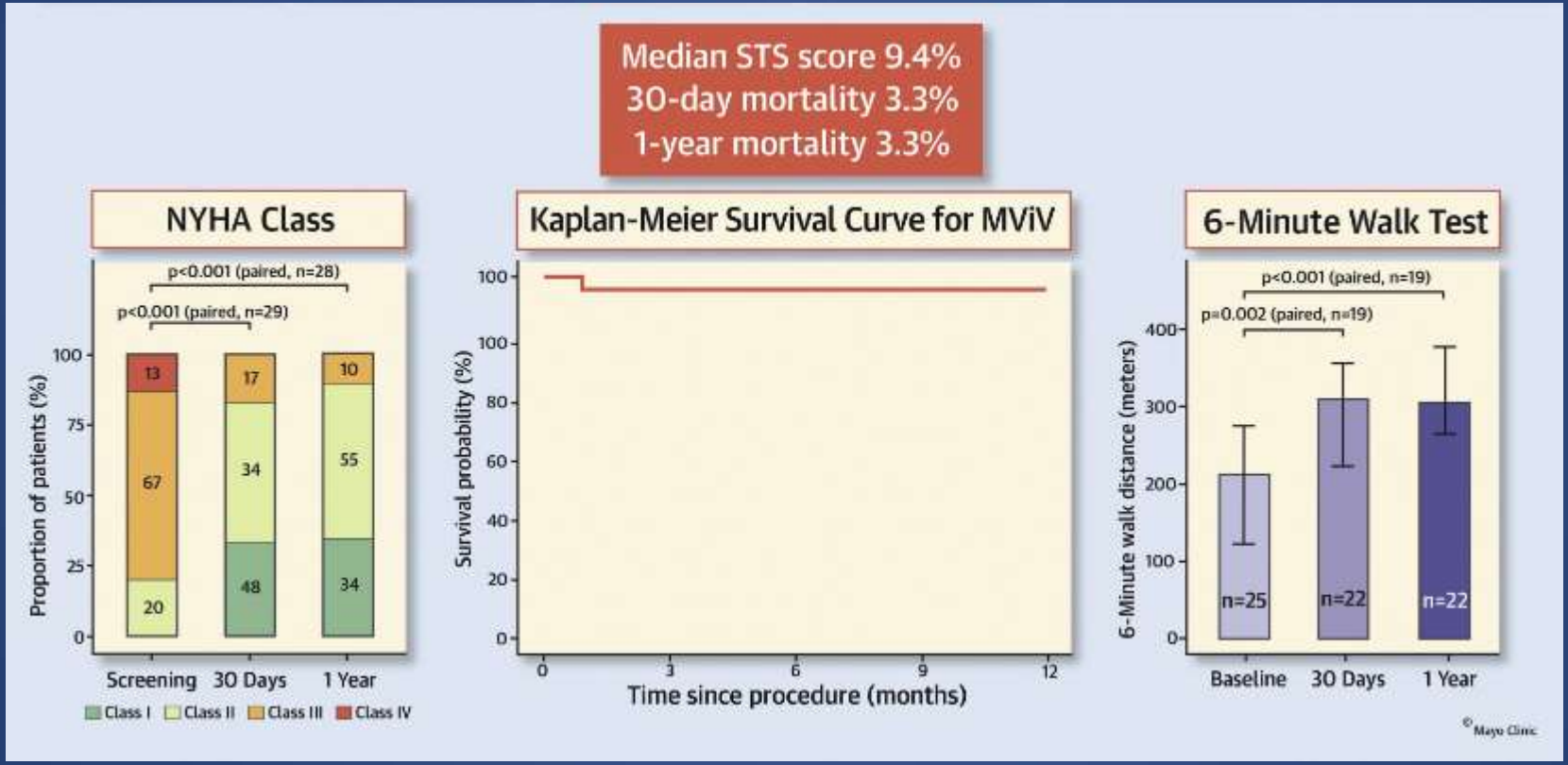
Mayra Guerrero, 2021 JACC
Prospective Evaluation of Transseptal TMVR for Failed Surgical Bioprostheses

MITRAL trial Valve-in-Valve Arm 1-Year Outcomes



Mayra Guerrero, 2021 JACC
Prospective Evaluation of Transseptal TMVR for Failed Surgical Bioprostheses

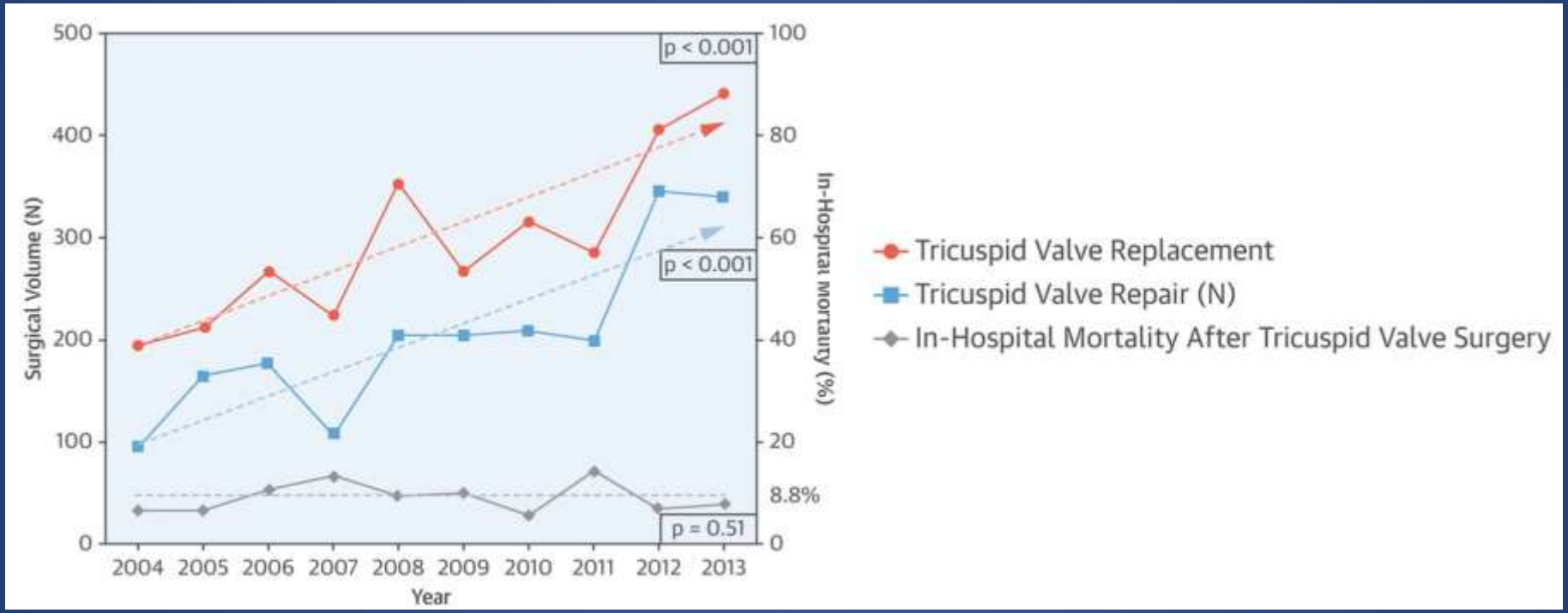
MITRAL trial Valve-in-Valve Arm 1-Year Outcomes



Mayra Guerrero, 2021 JACC
Prospective Evaluation of Transseptal TMVR for Failed Surgical Bioprostheses

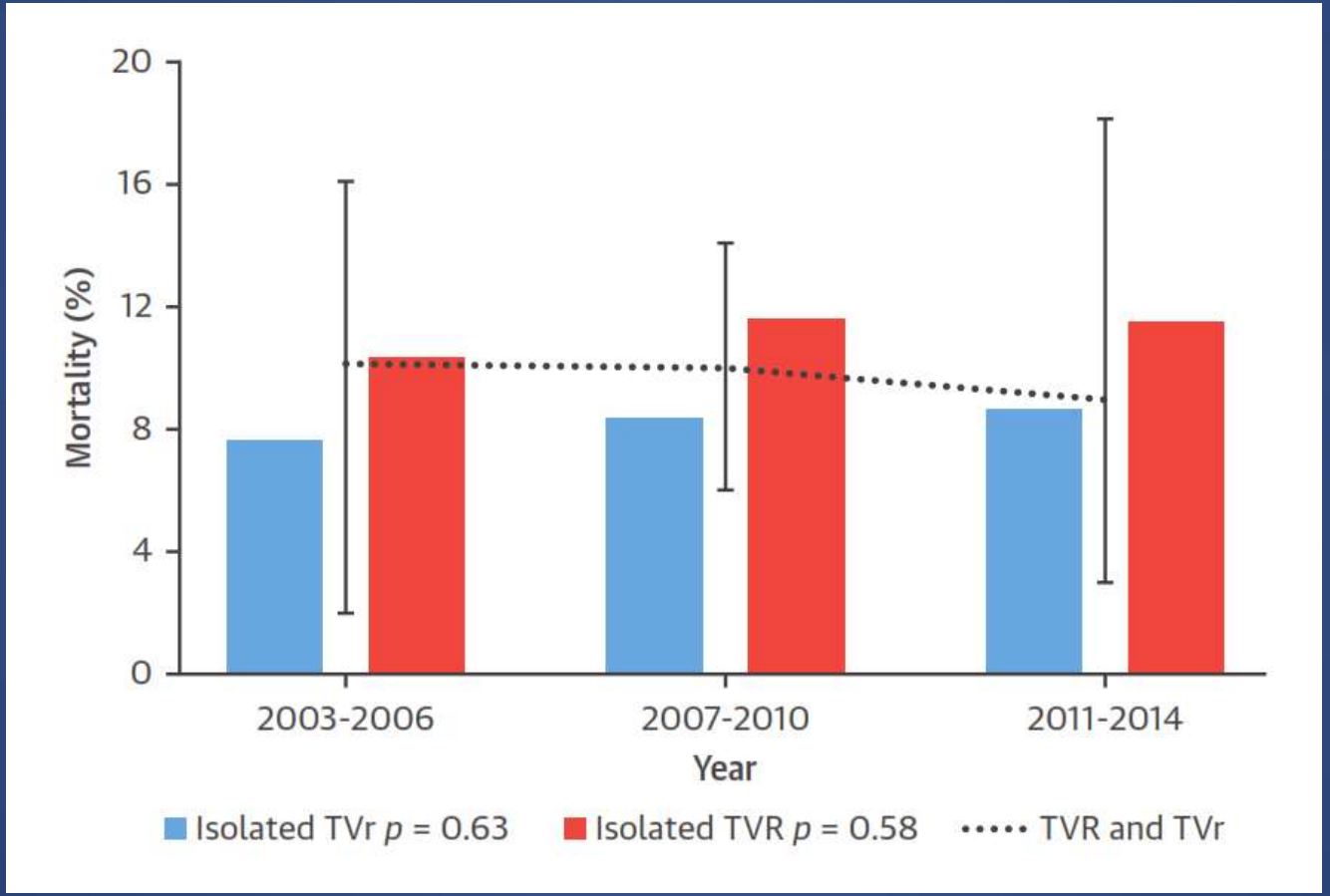
ViV: Tricuspid Valve

National Trends and Outcomes in Isolated Tricuspid Valve Surgery

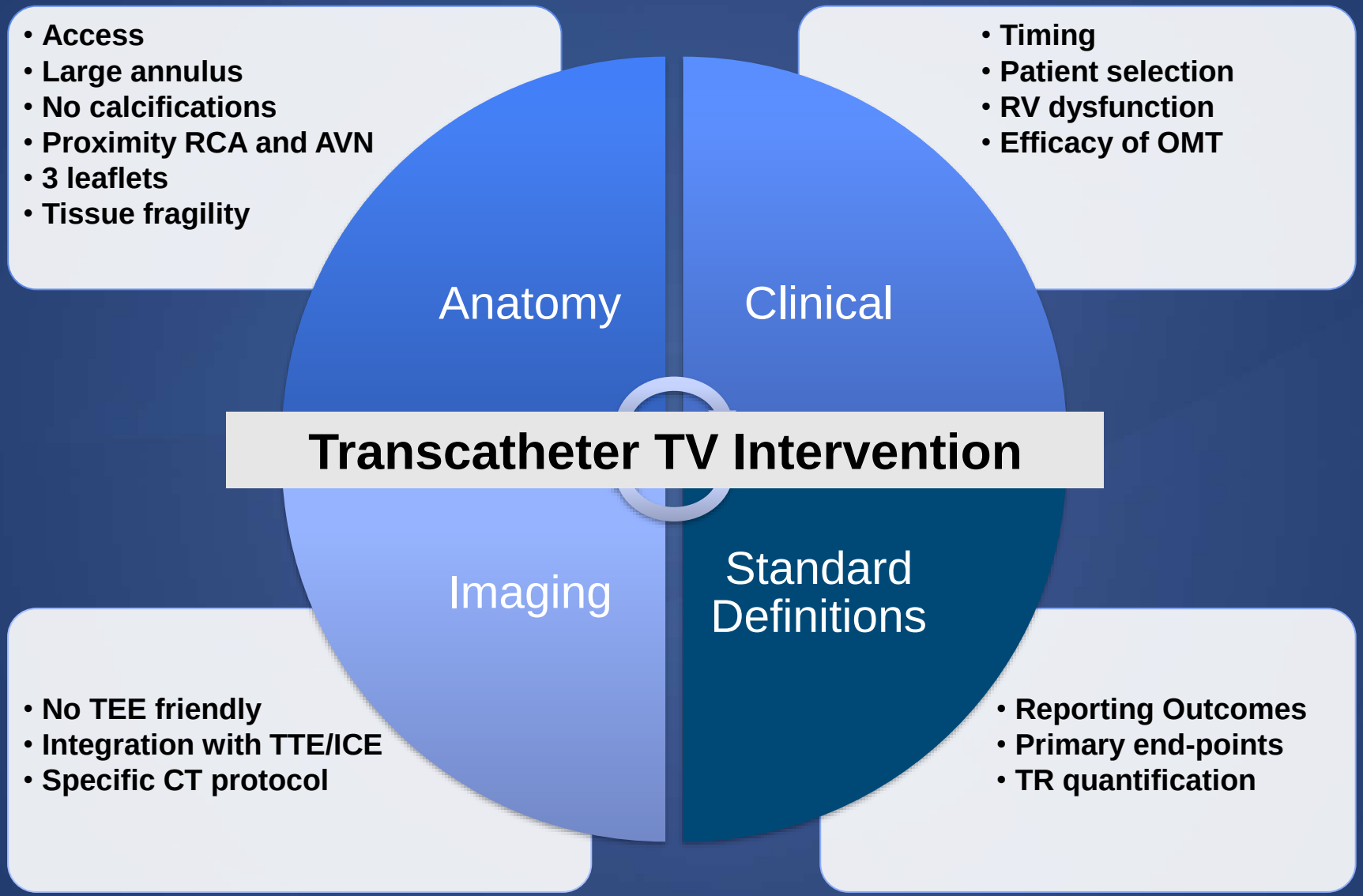


Zack, C.J. et al. J Am Coll Cardiol. 2017

Surgical Mortality – Isolated TVR/TVr



Alqahtani F, et al. J Am Heart Assoc 2017

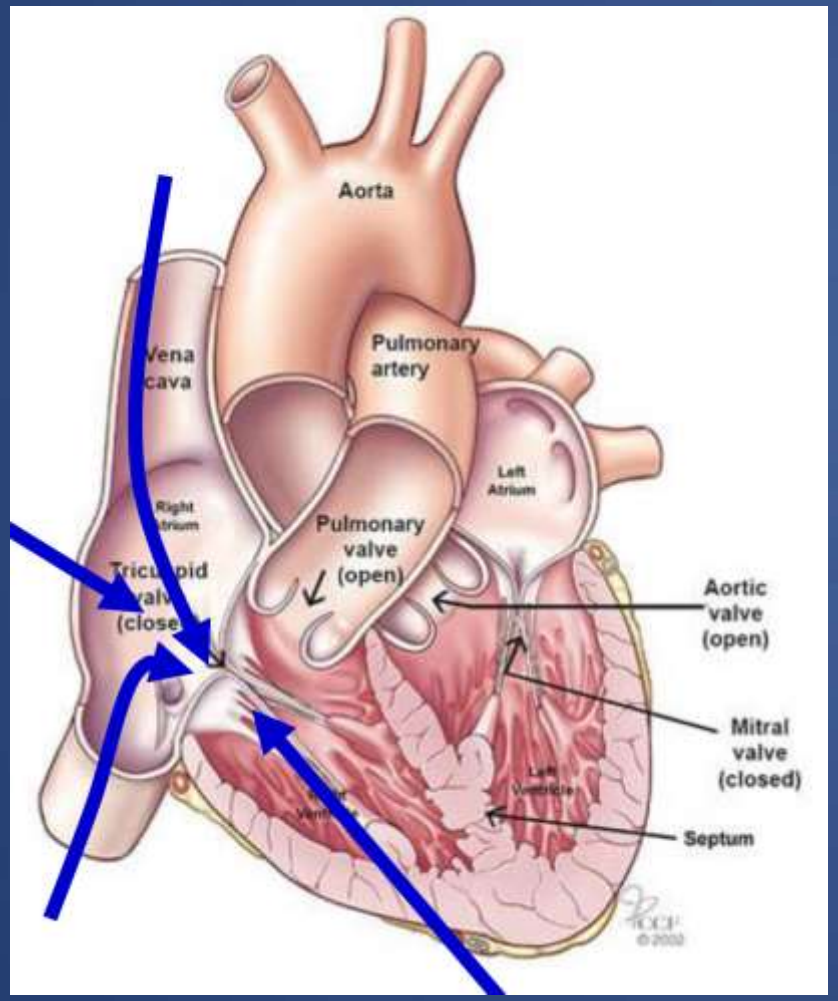

• Access
• Large annulus
• No calcifications
• Proximity RCA and AVN
• 3 leaflets
• Tissue fragility
• Timing
• Patient selection
• RV dysfunction
• Efficacy of OMT
Anatomy
Clinical
Transcatheter TV Intervention
Imaging
Standard Definitions
• No TEE friendly
• Integration with TTE/ICE
• Specific CT protocol
• Reporting Outcomes
• Primary end-points
• TR quantification

Challenges of Transcatheter TV Therapies

- Large tricuspid annulus size
- Nonplanar and elliptical annulus shape
- Fragility of tricuspid annular tissue and narrower annular shelf in comparison to mitral annulus
- Noncalcified annulus in secondary TR
- Angulation in relation to SVC and IVC
- Trabeculated RV, muscular bands and chordae tendinae
- Thin right ventricular free wall
- Proximity of AV node and right His bundle branch
- Proximity of the RCA to annulus and risk of coronary injury
- Risk of occlusion of coronary sinus, vena cava or outflow tract
- Slow-flow in right ventricle
- Patients with pacemaker or defibrillator leads

Rodés-Cabau et al. J Am Coll Cardiol. 2016;67:1829- 45

Transcatheter Tricuspid Solutions



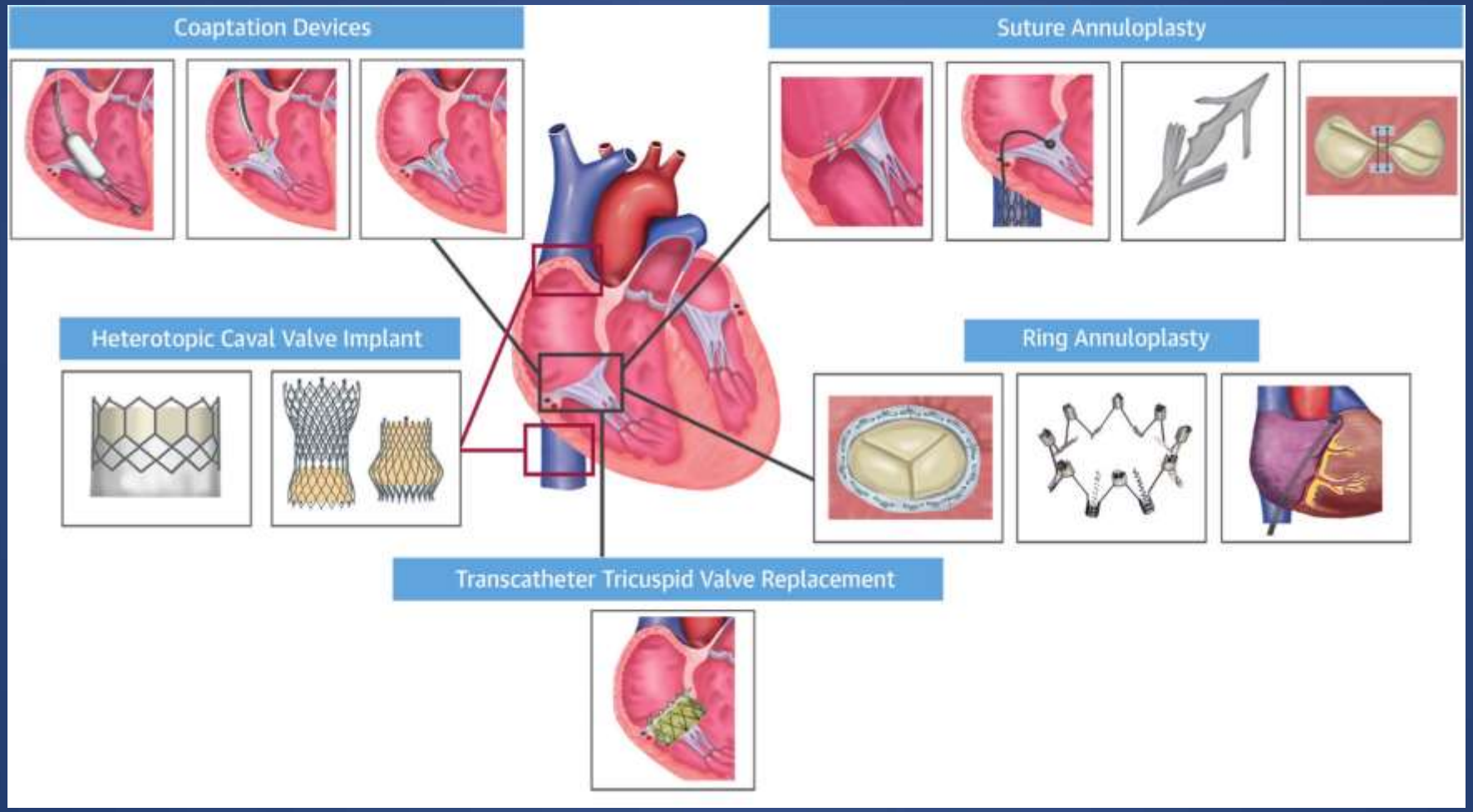
Approaches

1. Superior Vena Cava
2. Inferior Vena Cava
3. Transapical
4. Transatrial

Anatomic Target

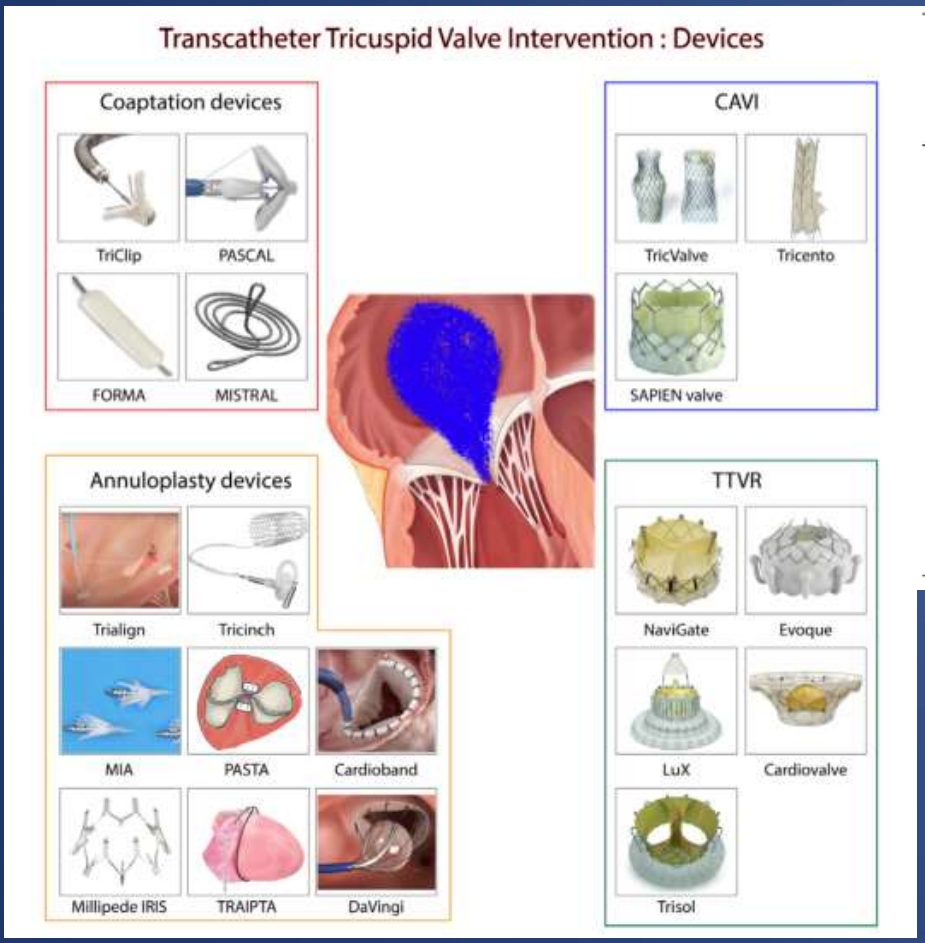
1. Leaflet
2. Annulus
3. IVC

Transcatheter Tricuspid Landscape



Asmarats et al. J Am Coll Cardiol. 2018;71(25):2935-56

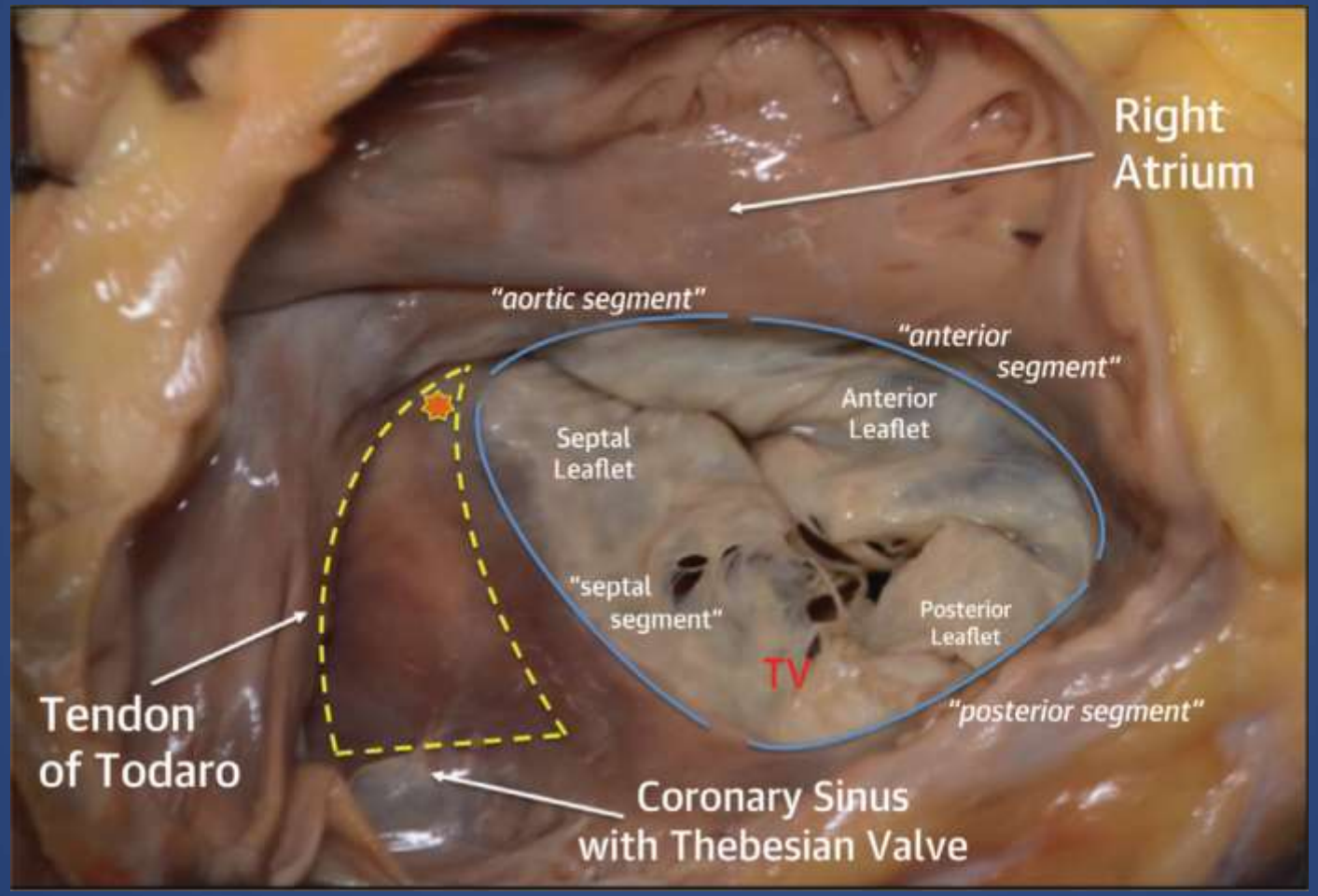
Transcatheter Tricuspid valve : Devices



Device	Study	*Baseline characteristics* Age, years	NYHA III/IV	CIED	Functional TR	*Procedural outcomes* Procedural success	Conversion to surgery	Residual TR ≥ grade 3	30-day mortality
TriClip	TriValve ($n = 249$)[46]	77 ± 9	238 (96)	74 (30)	223 (90)	192 (77)	1 (0.4)	57 (23)	–
	TRILUMINATE ($n = 85$)[43,49]	78 ± 8	64 (75)	12 (14)	71 (84)	76/85 (91)	0 (0)	36/83 (43)	0 (0)
Pascal	Fam et al. ($n = 28$)[50]	78 ± 6	28 (100)	1 (3)	26 (92)	24 (86)	0 (0)	4/26 (15)	2 (7)
	CLASP-TR ($n = 34$)[51]	76 ± 10	27 (79)	4 (12)	29 (88)	24 (80)	0 (0)	22/27 (81)	0 (0)
Forma	Perlmann et al. ($n = 18$)[54]	76 ± 10	17 (94)	3 (17)	18 (100)	16 (89)	1 (6)	7/16 (44)	0 (0)
	Kodali S. ($n = 29$)[53]	76 ± 8	25 (86)	7 (24)	29 (100)	27 (93)	3 (10)	–	2 (7)
Mistral	Planer et al. ($n = 7$)[55]	73 ± 7	–	1 (14)	7 (100)	7 (100)	0 (0.0)	–	0 (0)
Trialign	SCOUT I ($n = 15$)[58,59]	74 ± 7	10 (67)	0 (0)	15 (100)	15 (100)	0 (0)	–	0 (0)
TriCinch	PREVENT ($n = 24$)[62]	74 ± 8	14 (58)	–	–	18 (81)	–	~45%	0 (0)
Cardioband	TRI-REPAIR ($n = 30$)[67]	75 ± 7	25 (83)	4 (13)	30 (100)	30 (100)	0 (0)	5 (28)	0 (0)
	Davidson et al. ($n = 30$)[70]	77 ± 8	21 (70)	7 (23)	30 (100)	28 (93)	0 (0)	15 (55)	0 (0)
Caval devices	Lauten et al. ($n = 25$)[74]	74 ± 8	25 (100)	9 (36)	24 (96)	23 (92)	1 (4)	–	3 (12)
	TRICAVAL ($n = 14$)[83]	77 [68–82]	12 (86)	–	–	14 (100)	4 (29)	–	3 (21)
NaviGate	Hahn et al. (n = 30)[87]	78 [70–80]	24 (86)	9 (30)	30 (100)	26 (87)	2 (7)	0/26 (0)	3 (10)
Evoque	Fam et al. ($n = 25$)[93]	76 ± 3	22 (88)	9 (36)	19 (76)	23 (92)	0 (0)	1 (4)	0 (0)
LuX valve	Lu et al. ($n = 12$) (96)l	69 [66–74]	12 (100)	5 (42)	–	12 (100)	–	1 (8)	0 (0)

Progress in Cardiovascular Diseases 69 (2021) 89–100

TV and Surrounding Structures



Asmarats et al. J Am Coll Cardiol. 2018;71(25):2935-56

Etiologies of TR

Morphological Classification	Disease Subgroup	Specific Abnormality
Primary leaflet abnormality: 25%	Congenital	Ebstein's anomaly Tricuspid valve tethering associated with perimembranous VSD and VSA Other (giant right atrium)
	Acquired disease	Carcinoid Degenerative (myxomatous) Endocarditis Endomyocardial fibrosis Iatrogenic (pacing leads, RV biopsy) Rheumatic Toxins Trauma Other (e.g., ischemic papillary muscle rupture)
Secondary ("functional"): 75%	Left heart disease	LV dysfunction or valve disease
	Right ventricular dysfunction	RV cardiomyopathy (e.g., ARVD) RV ischemia RV volume overload
	Pulmonary Hypertension	Chronic lung disease Left-to-right shunt Pulmonary thromboembolism
	Right atrial abnormalities	Atrial fibrillation
Other	Post-operative	Recurrent TR post-surgical intervention

TTVI sytems selection

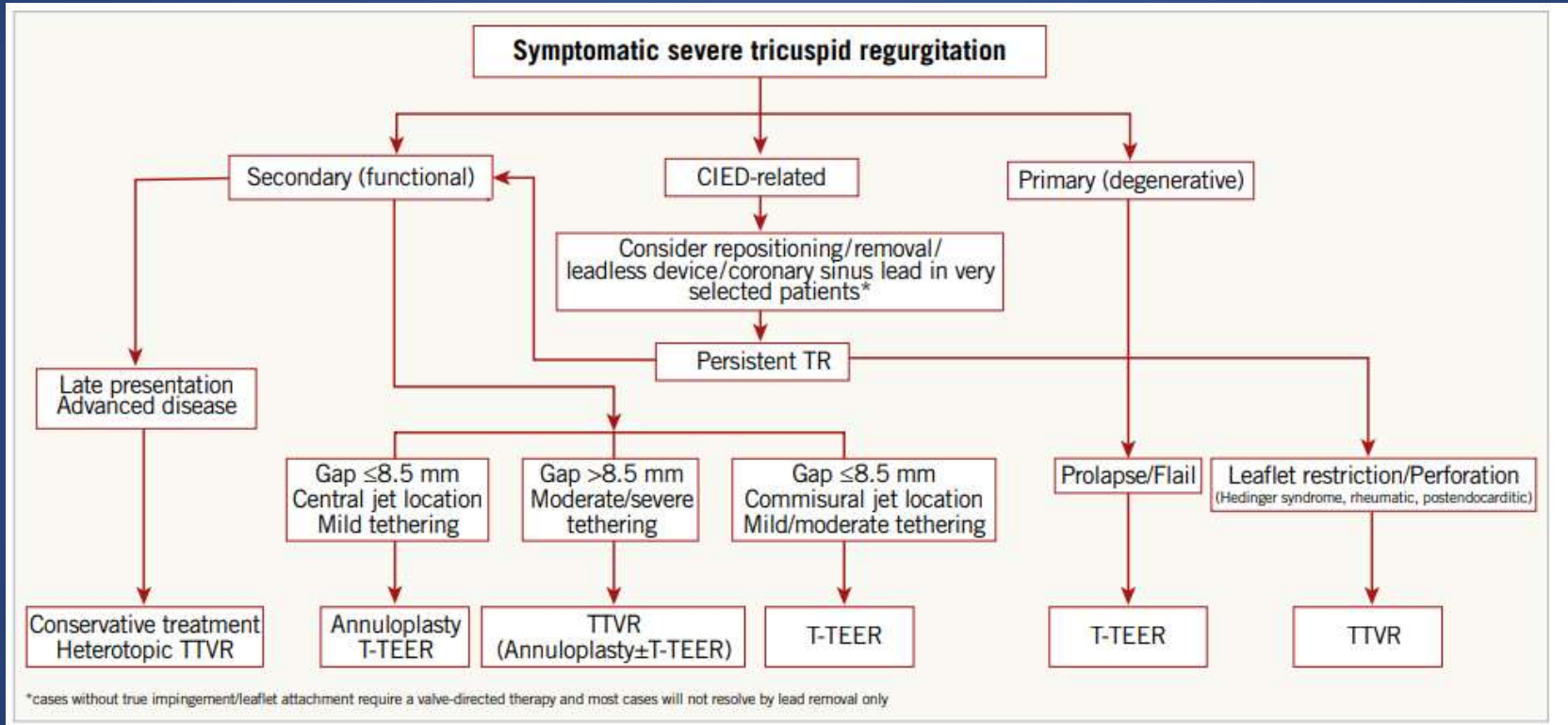


Figure 6. *Proposed algorithm for the selection of TTVI systems. CIED: cardiac implantable electronic device; T-TEER: tricuspid transcatheter edge-to-edge repair; TTVR: transcatheter tricuspid valve replacement*

EuroIntervention 2021;17:791-808

Criteria for device selection

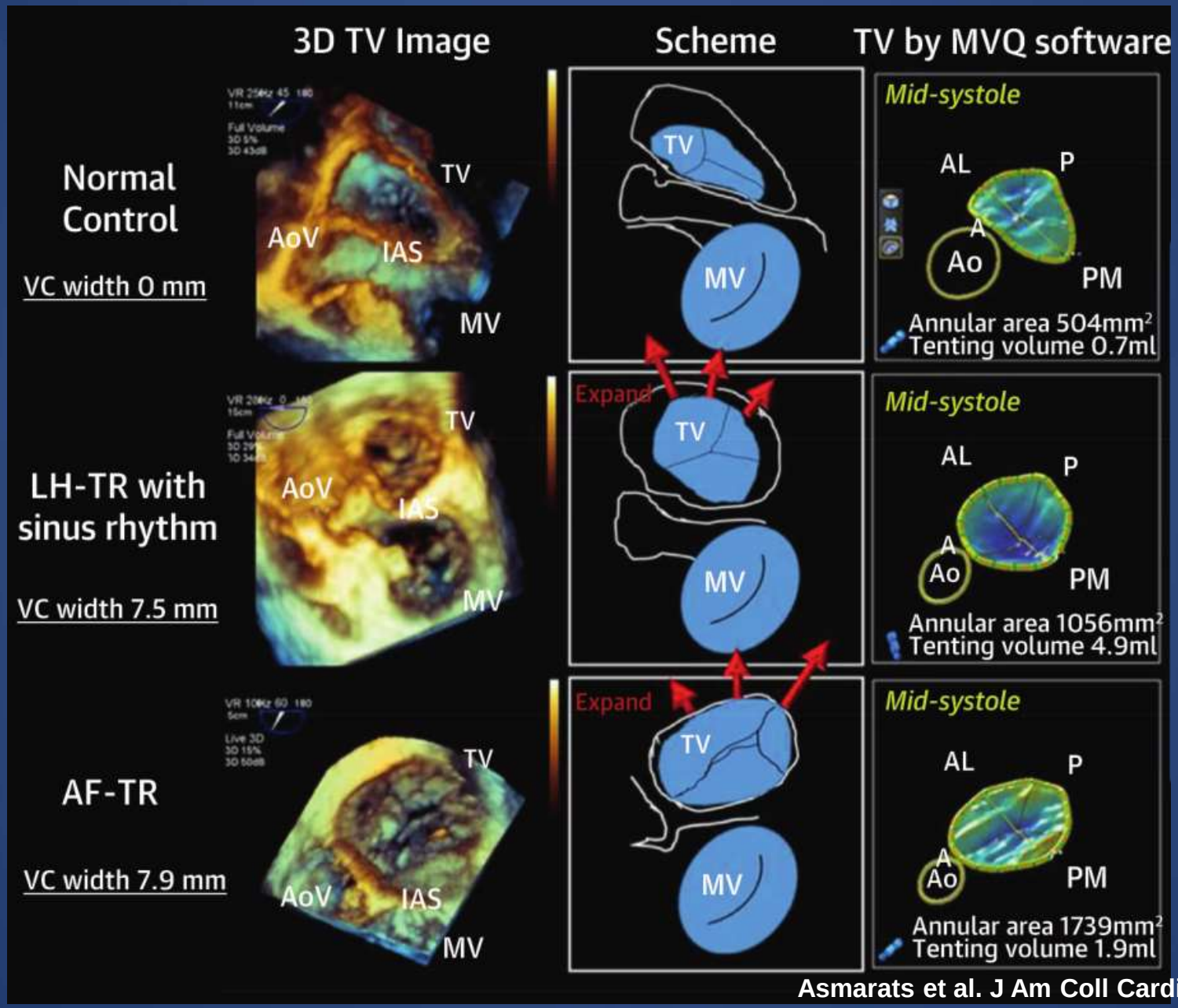
Table 3. Anatomical criteria for device selection.

Strategy	Favourable anatomy	Feasible anatomy	Unfavourable anatomy
Leaflet approximation	Small septolateral gap ≤7 mm[10] Anteroseptal jet location Confined prolapse or flail Trileaflet morphology	Septolateral coaptation gap >7 but ≤8.5 mm[65] Posteroseptal jet location Non-trileaflet morphology Incidental CIED RV lead (i.e., without leaflet impingement)	Large septolateral coaptation gap >8.5 mm[65] Leaflet thickening/shortening (rheumatic, carcinoid)/perforation Dense chordae with marked leaflet tethering Anteroposterior jet location Poor echocardiographic leaflet visualisation CIED RV lead leaflet impingement Unfavourable device angle of approach
Annuloplasty	Annular dilatation as primary mechanism of TR Mild tethering (tenting height <0.76 cm, tenting area<1.63 cm², tenting volume [3D] <2.3 mL)[110,111] Central jet location Sufficient landing zone for anchoring	Moderate tethering (tethering height ≥0.76 cm but <1.0 cm, tenting area >1.63 but <2.5 cm², tenting volume [3D] ≥2.3 mL but ≤3.5 mL)[110,111] Incidental CIED RV lead (i.e., without leaflet impingement)	Excessive annular dilatation (exceeding device size) Severe tethering (tethering height >1.0 cm, tenting volume >3.5 mL). Poor echocardiographic annular visualisation[110,111] Annular proximity of RCA CIED RV lead leaflet impingement
Orthotopic valve implantation	Previous surgical repair or bioprosthetic valve replacement Leaflet thickening/shortening (rheumatic, carcinoid) Incidental CIED RV lead (i.e., without leaflet impingement) Any leaflet morphology	Large coaptation gap CIED RV lead leaflet impingement	Excessive annular dilatation (exceeding device size) Unfavourable device angle of approach Severe right ventricular dysfunction
Heterotopic valve implantation	Appropriate caval diameters (and intercaval distance) No option for direct valve treatment		Proximity of the RA to the orifice of the liver veins (<10-12 mm) Severely increased pulmonary artery and RA pressures due to the risk of fracture of bicaval valved stents

3D: three-dimensional; CIED: cardiac implantable electronic device; RA: right atrium; RCA: right coronary artery; RV: right ventricular; TR: tricuspid regurgitation

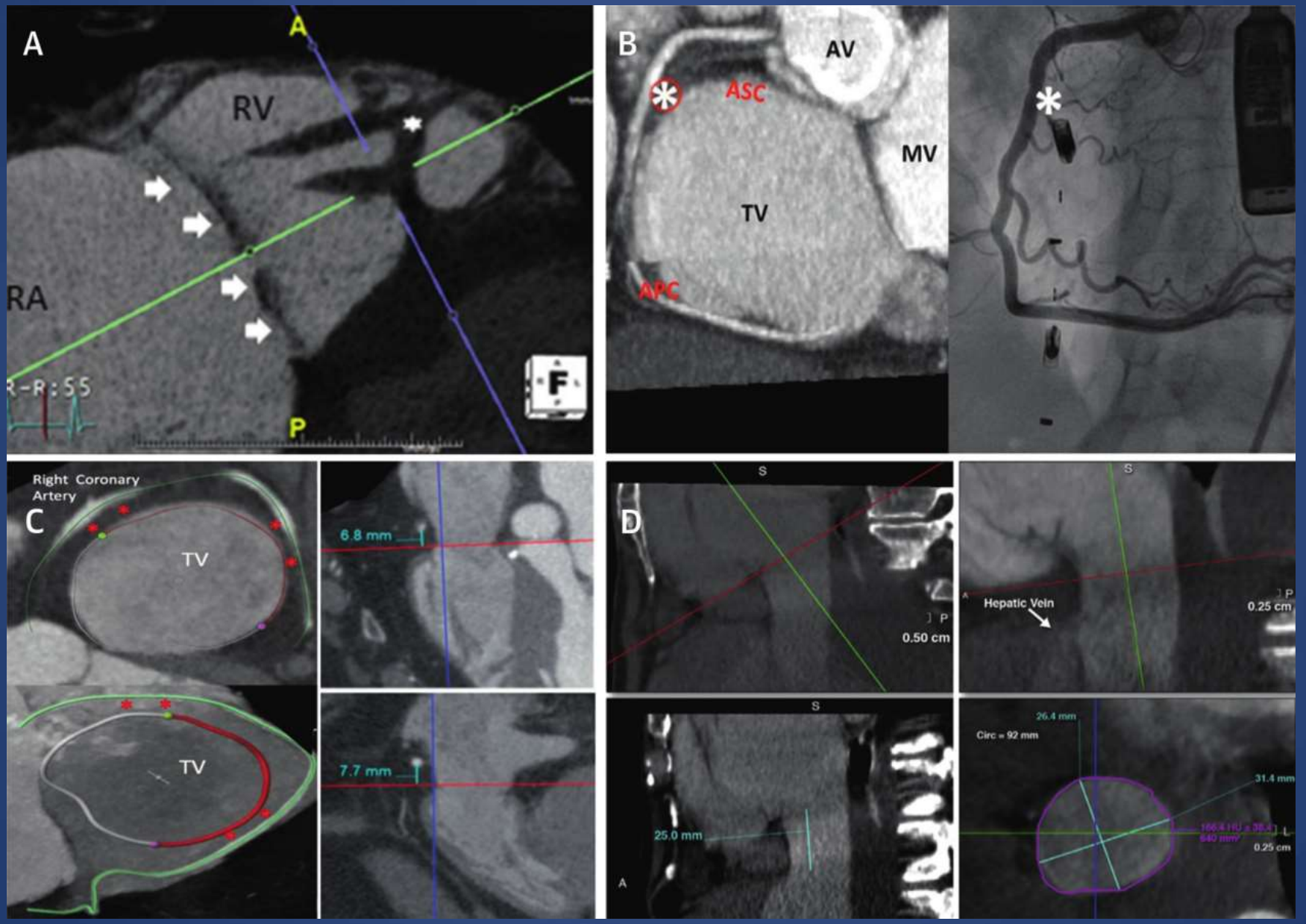
EuroIntervention 2021;17:791-808

Pathoanatomy of Functional TR



Asmarats et al. J Am Coll Cardiol. 2018;71(25):2935-56

CT Pre-Procedural Workup



Asmarats et al. J Am Coll Cardiol. 2018;71(25):2935-56

Key Considerations During Orthotopic TTVR

- Tricuspid annular dimensions (anteroposterior and septal-lateral diameters, perimeter, area)
- Right internal jugular vein and SVC size
- Course of the RCA relative to the TA
- Distance from RCA to the anterior and posterior tricuspid leaflet insertion
- Risk for RVOT obstruction

Orthotopic TTVR
NaviGate Tricuspid Valved Stent

Components Specifications

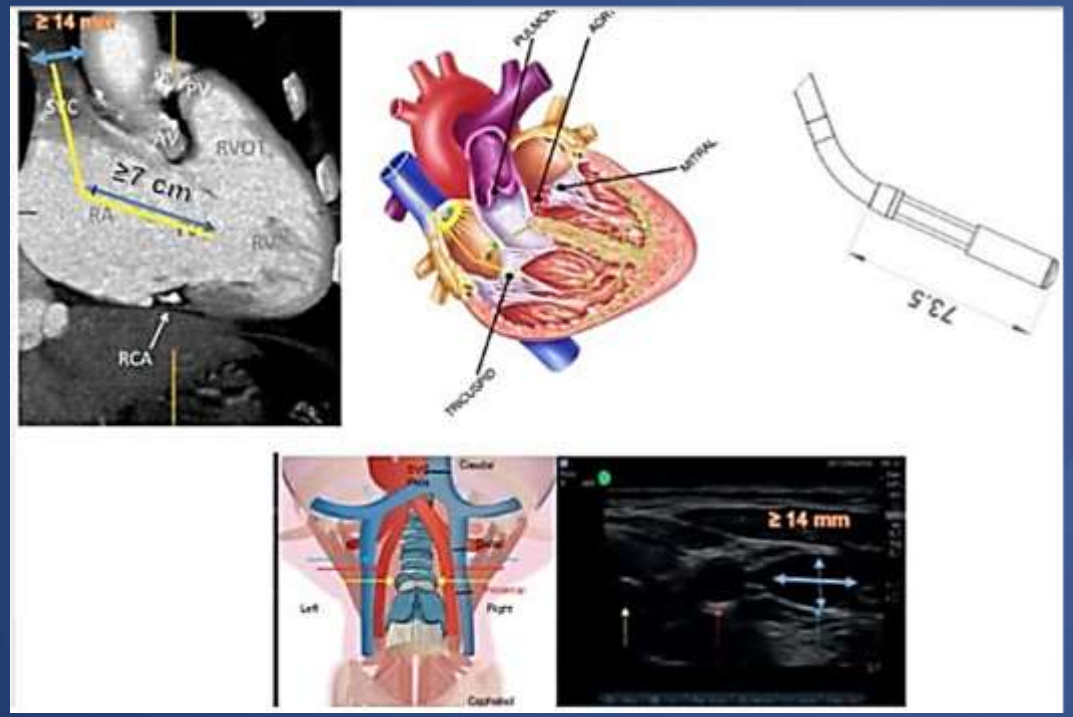
- Temperature Shape Memory NiTinol Tapered Stent
- Height profile 21mm, Truncated Cone configuration
- Annular Winglets for secure anchoring of TV annulus and tricuspid valve leaflets
- Sizes = 36mm, 40mm, 44mm, 48mm, and 52mm.
- Chemically Preserved Xenogeneic Pericardium

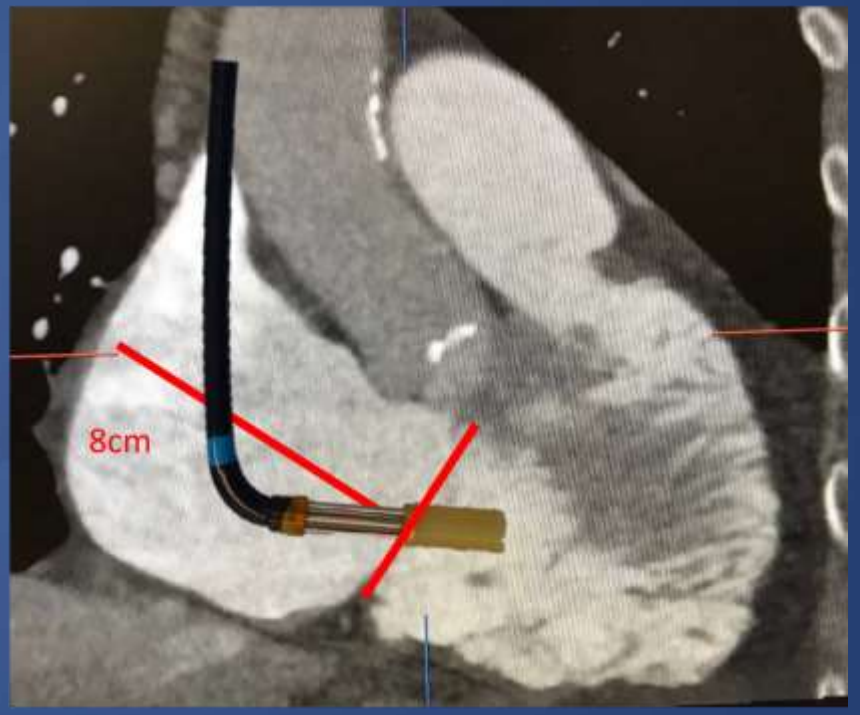
Delivery System

- Presently 35F at the distal capsule
- 24F catheter shaft
- Two degrees of motion at tip
- 80° Articulation
- Controlled Valve Release
- The delivery use the same valve configuration

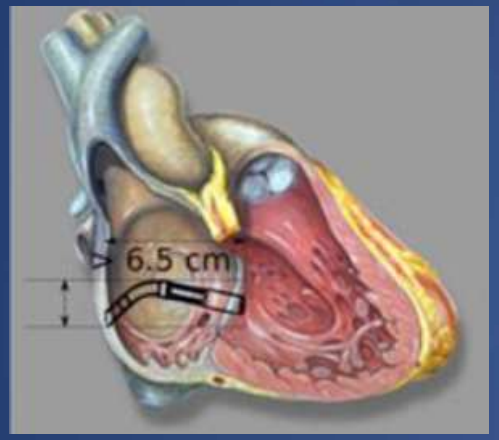
Asmarats et al. J Am Coll Cardiol. 2018;71(25):2935-56

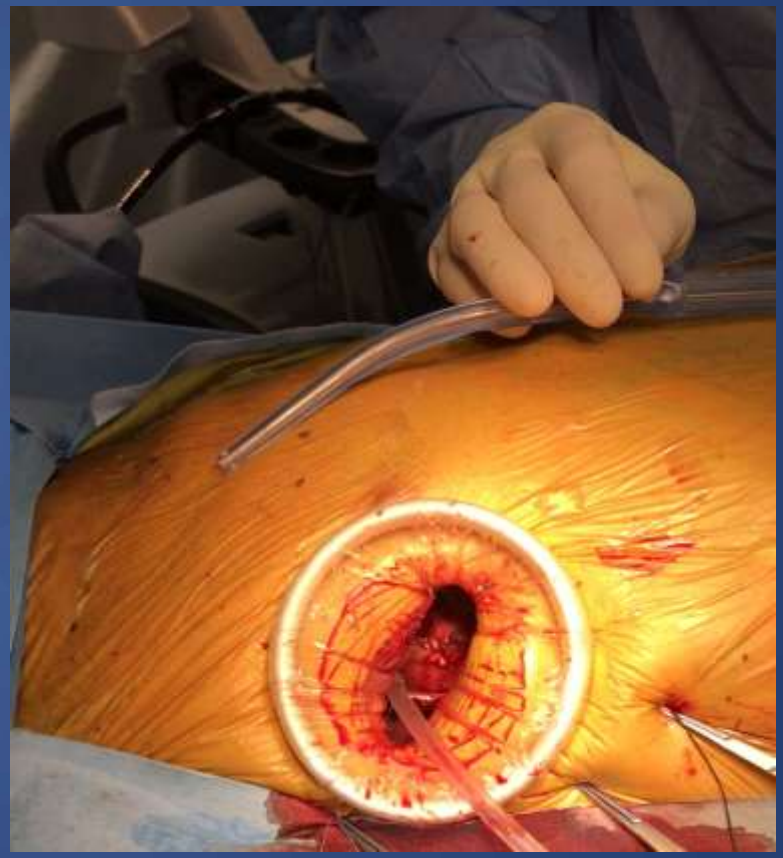
Orthotopic TTVR
Trans Jugular Requirements

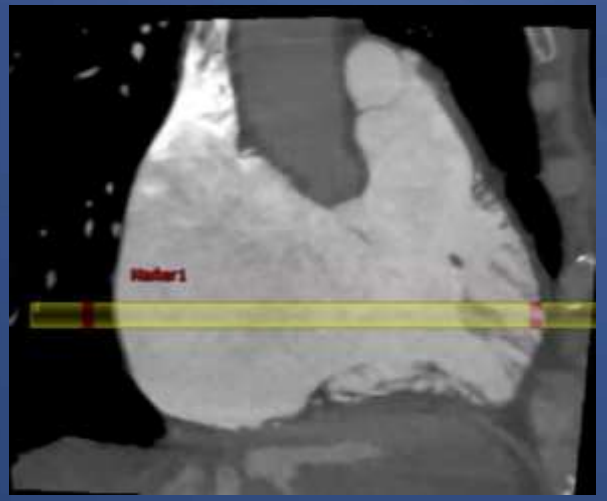




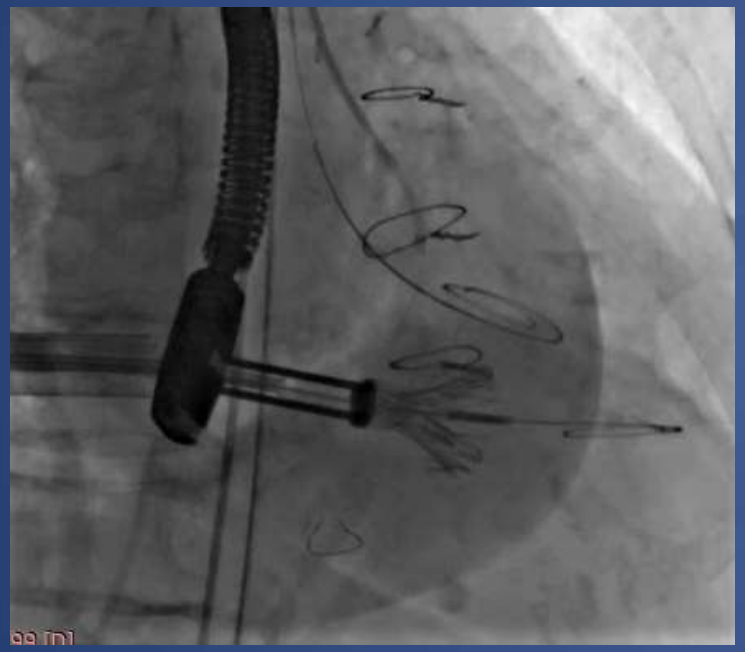
Orthotopic TTVR
Right Atrial Access



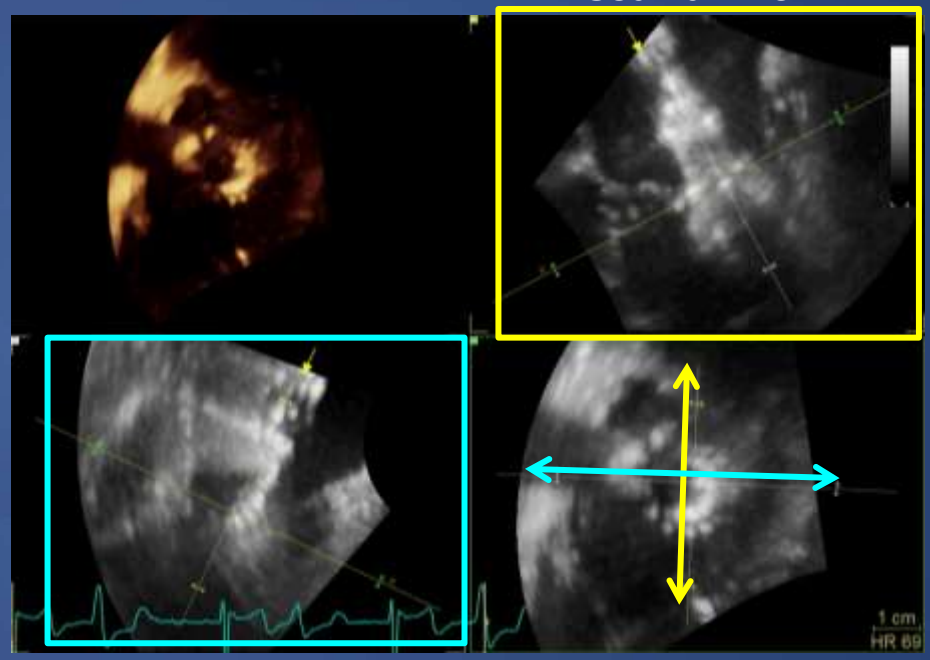




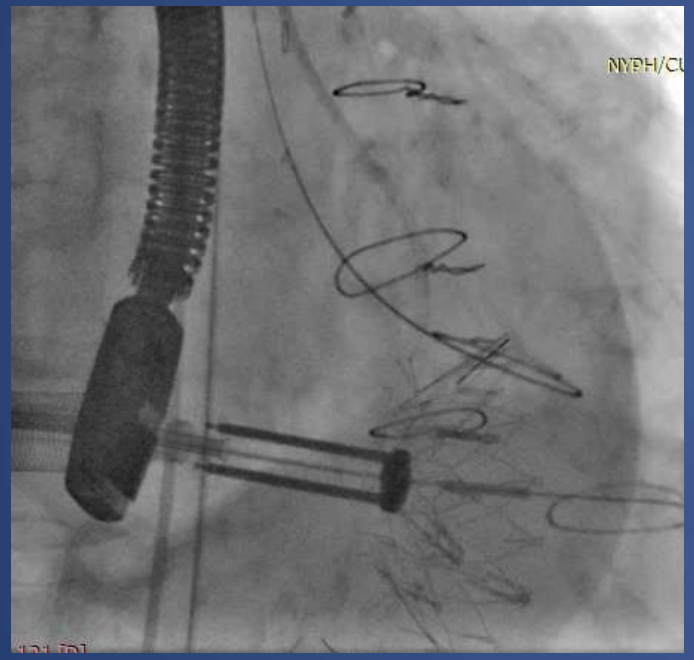
Initial valve deployment with RCA injection

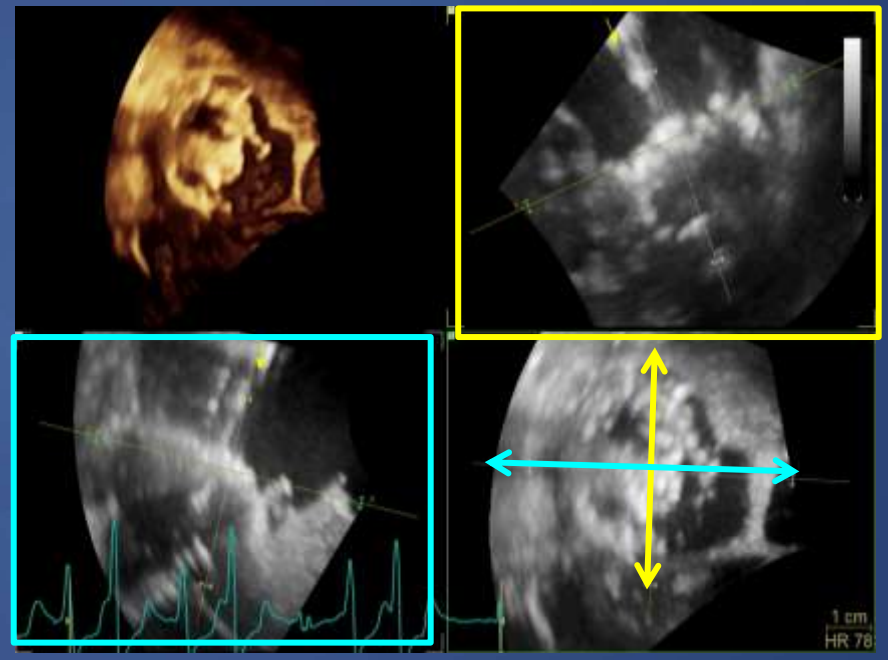


Retracting the capsule:
Exposing Ventricular Tines

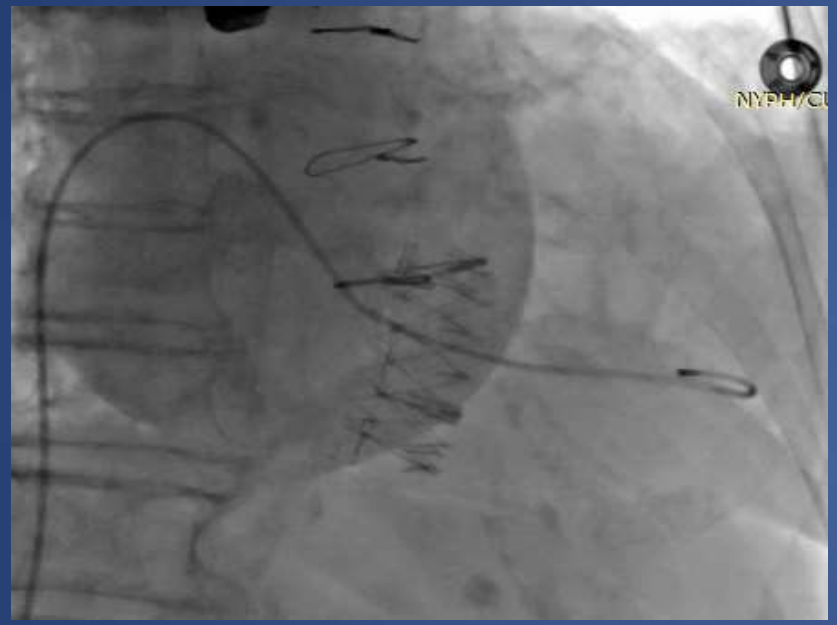


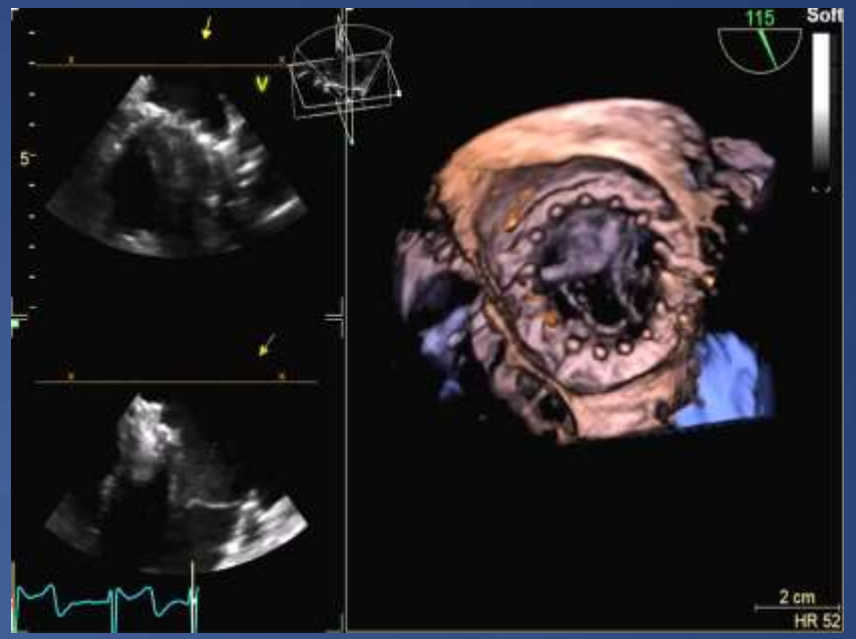
Valve Release: Complete Deployment

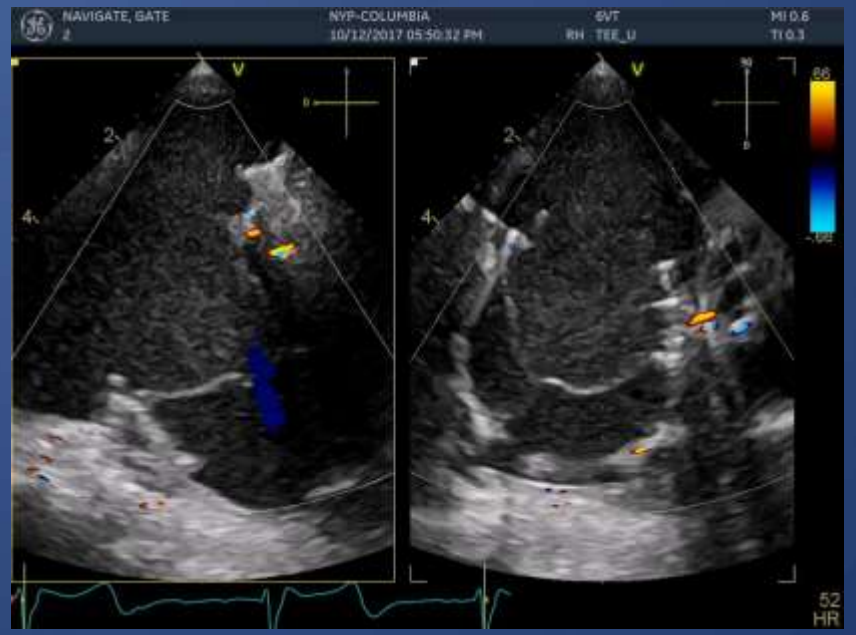




Final Result

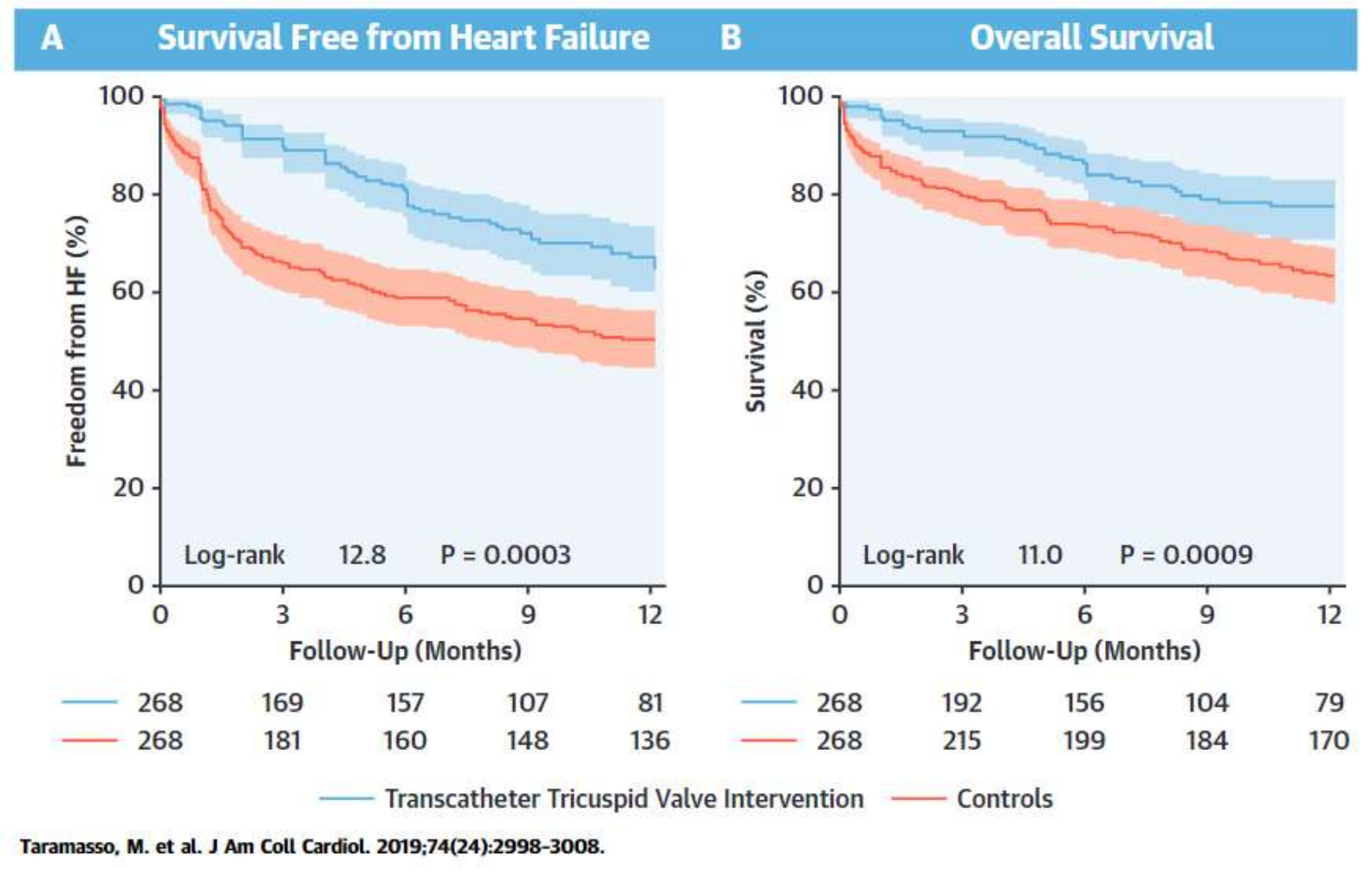






- Trivial central and trivial paravalvular regurgitation
- Peak/mean transtricuspid gradient = 1.5 and 0.3 mmHg

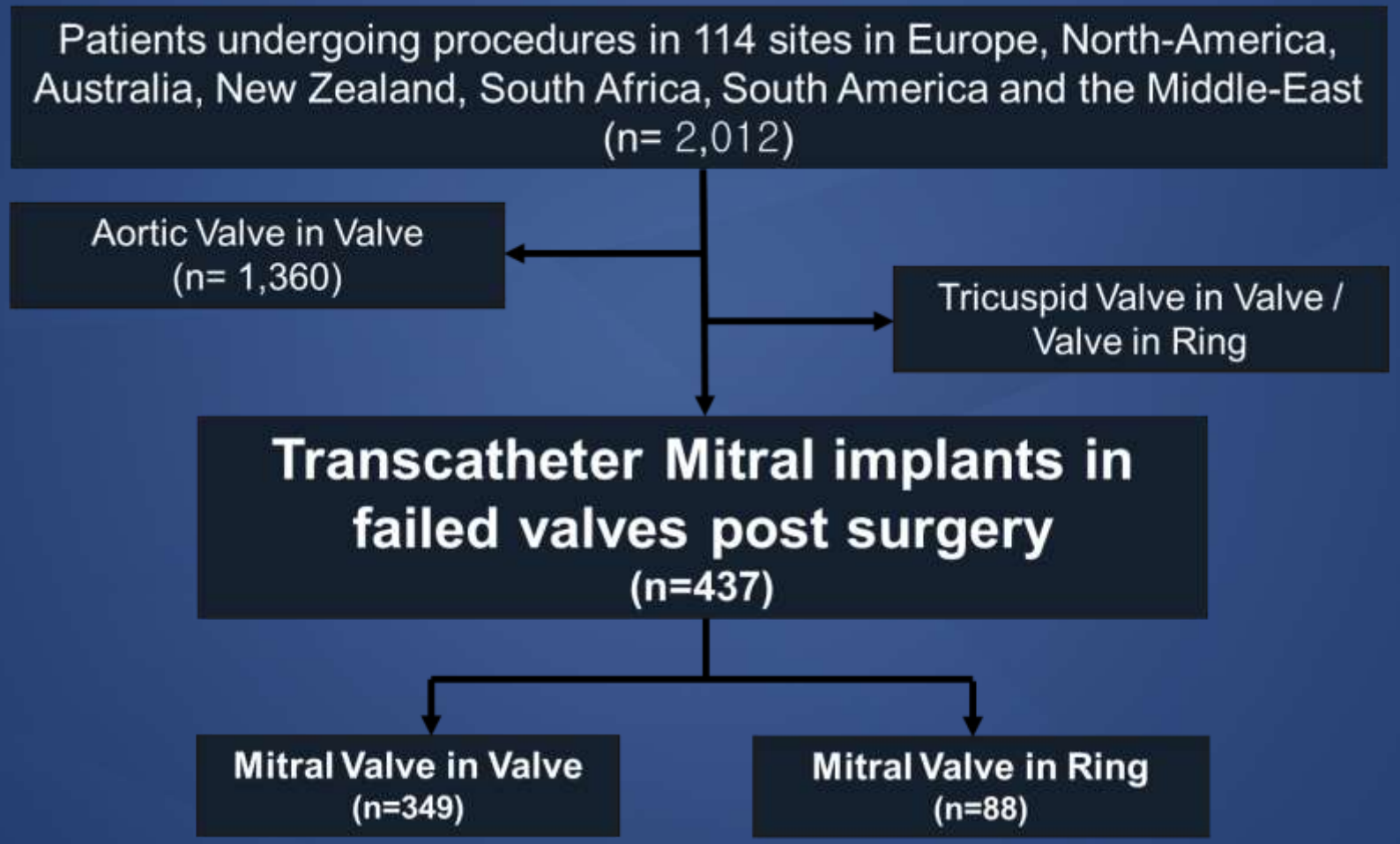
Outcomes : Transcatheter *vs.* Medical treatment



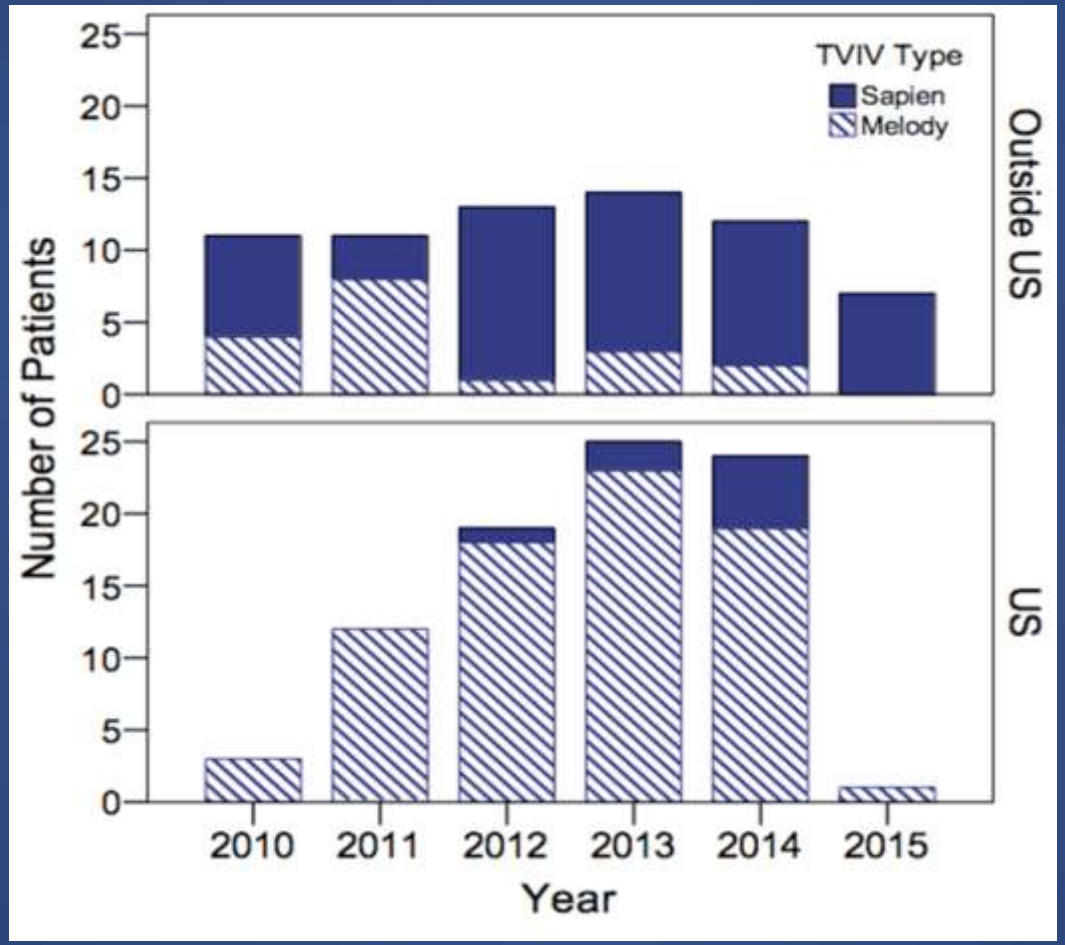
Taramasso, M. et al. J Am Coll Cardiol. 2019;74(24):2998-3008.

ViV Replacement for Bioprosthetic TV Degeneration

VIVID Registry – DataLock 2015



Transcatheter Tricuspid VIV



McElhinney D et al. Circulation. 2016;133:1582-1593.

VIVID Registry –TVIV
Baseline Characteristics

Variable	All Patients N=156	Melody Patients N=94	Sapien Patients N=58	P Value
Patient age (yrs)	40 (5-84)	27 (5-84)	53 (8-81)	<0.001
Etiology of Original TV Disease (prior to TVR)				<0.001
Congenital	87 (56%)	63 (67%)	21 (36%)	
Acquired	69 (44%)	31 (33%)	37 (64%)	
Atrial fibrillation or flutter	60 (38%)	36 (38%)	24 (41%)	0.71
Acute/chronic renal insufficiency	20 (13%)	9 (10%)	10 (17%)	0.17
COPD/Lung disease	10 (6%)	6 (6%)	4 (7%)	0.89
Prior history of endocarditis	31 (20%)	14 (15%)	16 (30%)	0.03
Existing permanent pacemaker	62 (39%)	37 (39%)	22 (38%)	0.91
Epicardial	38 (24%)	23 (25%)	14 (24%)	
Transvenous	24 (15%)	14 (15%)	8 (14%)	

McElhinney D et al. Circulation. 2016;133:1582-1593.

VIVID Registry –TVIV

TV function and Prosthesis-Related Data

Variable	All Patients N=156	Melody Patients N=94	Sapien Patients N=58	P Value
Age of TV bioprosthesis (yrs) (N=146)	7.4 (1-38)	7.2 (1.2-34)	8.0 (1-38)	0.37
Labeled size of TV bioprosthesis (mm) (N=146)	28 (18-35)	27 (18-35)	31 (24-33)	<0.001
29mm or larger	74 (51)	33 (38%)	39 (68%)	<0.001
TR severity				0.06
None/trivial	19 (12%)	7 (8%)	12 (20%)	
Mild	24 (15%)	14 (15%)	9 (16%)	
Moderate	45 (29%)	26 (28%)	16 (28%)	
Severe	68 (44%)	47 (50%)	21 (36%)	
Mean Doppler TV inflow gradient (mmHg)	9 (2-29)	9 (2-29)	9 (2-24)	0.86
10-14	59 (38%)	37 (39%)	19 (33%)	
≥15	15 (10%)	9 (10%)	6 (10%)	

McElhinney D et al. Circulation. 2016;133:1582-1593.

VIVID Registry –TVIV

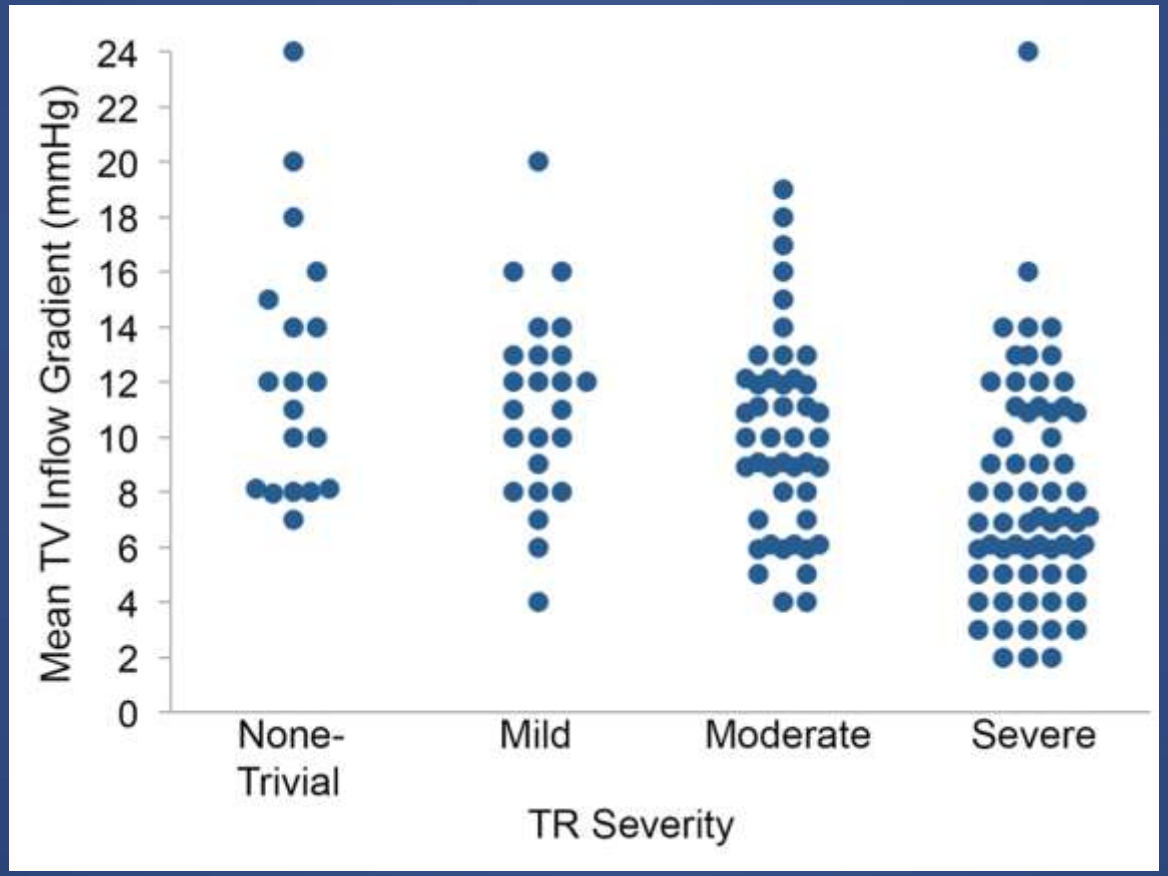
TV function and Prosthesis-Related Data

Variable	All Patients N=156	Melody Patients N=94	Sapien Patients N=58	P Value
Invasive Pressure Measurements (mmHg)				
Right atrial mean pressure, N=136	16 (6-37)	17 (6-30)	15 (6-37)	0.5
Right ventricular end-diastolic pressure, N=127	8 (1-22)	9 (1-22)	8 (2-16)	0.4
Right ventricular systolic pressure, N=132	30 (12-92)	29 (12-70)	33 (14-74)	0.5

McElhinney D et al. Circulation. 2016;133:1582-1593.

VIVID Registry –TVIV

TV function and Prosthesis-Related Data

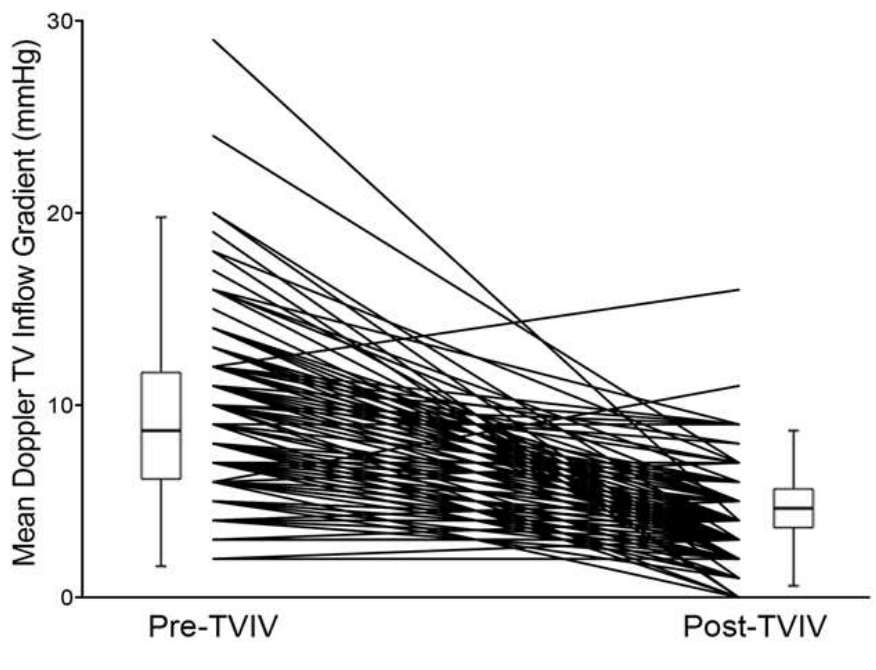


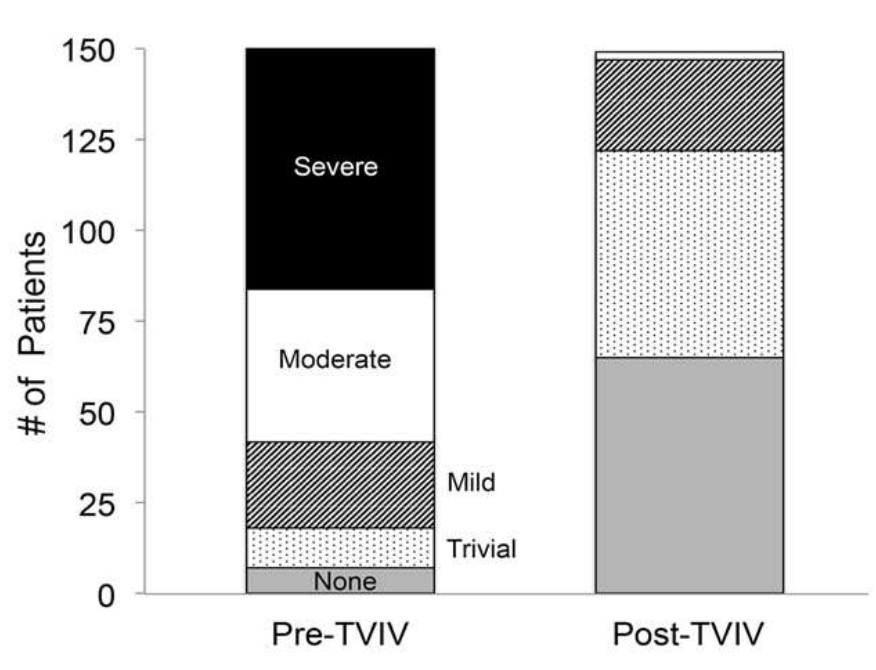
McElhinney D et al. Circulation. 2016;133:1582-1593.

VIVID Registry –TVIV
Procedural Variables for Attempted TVIV

Variable	All Patients N=152	Melody Patients N=94	Sapien Patients N=58	P Value
Vascular access				0.01
Femoral vein	105 (69%)	65 (69%)	40 (69%)	
Jugular vein	42 (28%)	29 (31%)	13 (22%)	
Surgical via right atrium	5 (3%)	0 (0%)	5 (9%)	
General anesthesia	137 (90%)	87 (93%)	50 (88%)	0.32
Intraprocedural echocardiography performed	125 (82%)	77 (82%)	48 (83%)	0.91
Transthoracic	10 (7%)	8 (9%)	2 (4%)	
Transesophageal	77 (51%)	37 (39%)	42 (72%)	<0.001
Intracardiac	32 (21%)	29 (31%)	3 (5%)	<0.001
Rapid pacing used during implantation	33 (22%)	2 (2%)	31 (54%)	<0.001
Predilation/balloon sizing before implantation	81 (53%)	61 (65%)	20 (35%)	<0.001
Bioprosthetic valve presented before TVIV	9 (6%)	4 (4%)	5 (9%)	0.30
Valve postdilated	40 (26%)	38 (40%)	2 (4%)	<0.001

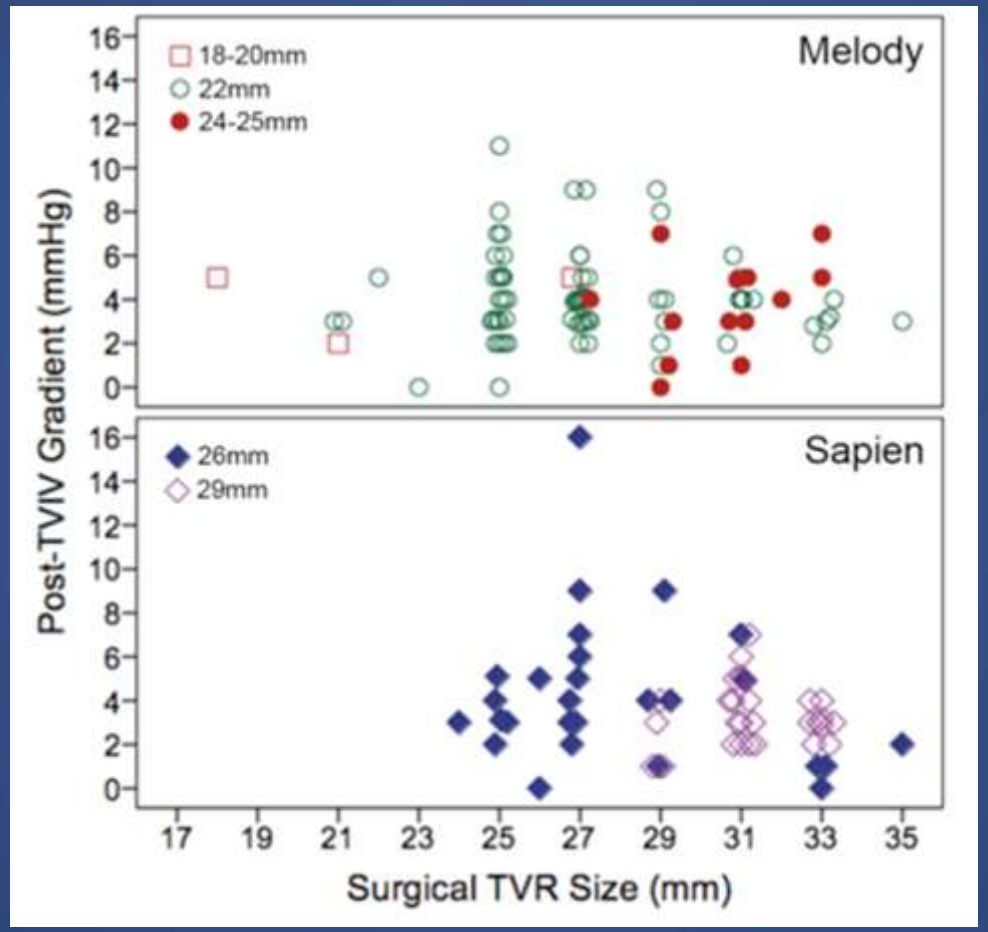
VIVID Registry –TVIV
Mean Doppler RA-RV gradient





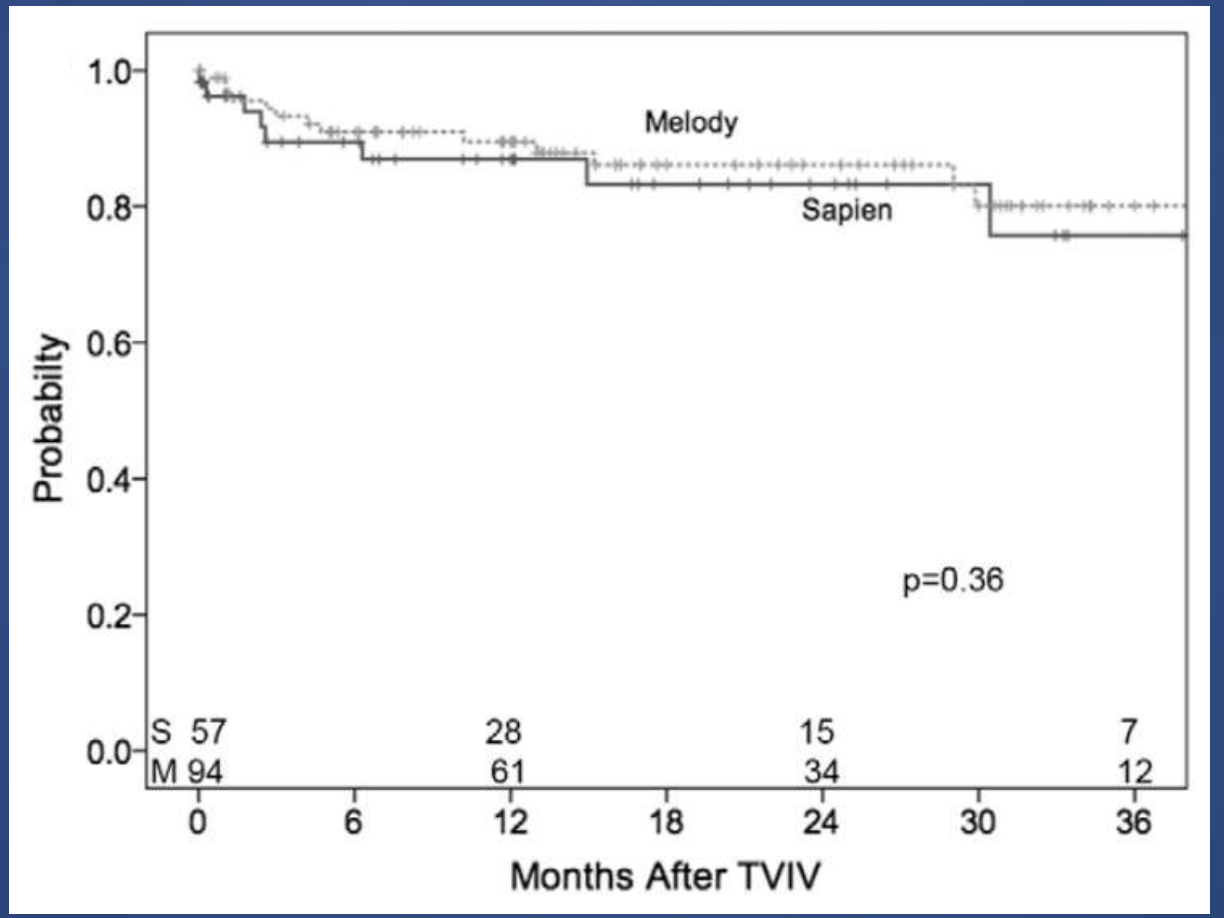
McElhinney D et al. Circulation. 2016;133:1582-1593.

VIVID Registry –TVIV
Post-TVIV RA-RV gradient



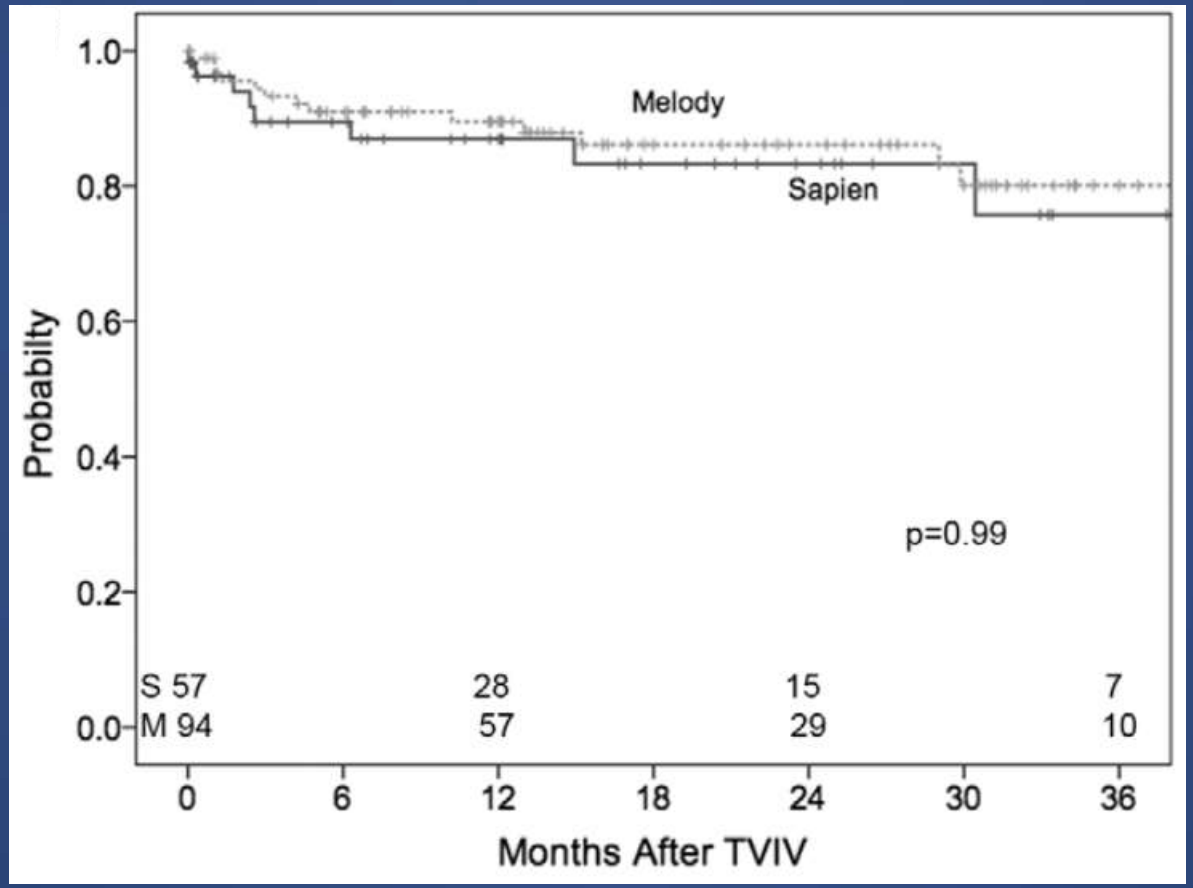
McElhinney D et al. Circulation. 2016;133:1582-1593.

VIVID Registry –TVIV
Survival after Tricuspid ViV



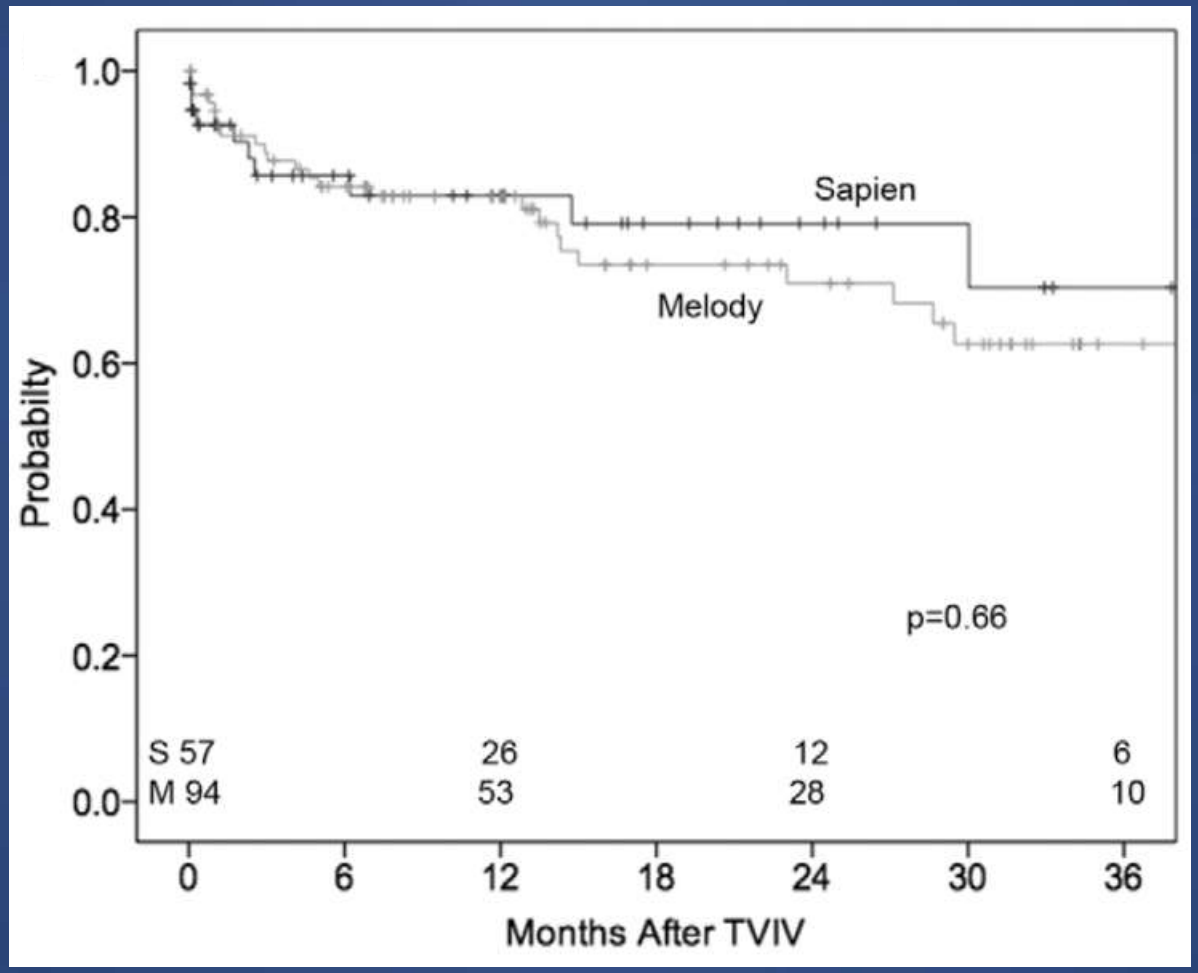
McElhinney D et al. Circulation. 2016;133:1582-1593.

VIVID Registry –TVIV
Survival free from TVIV reintervention



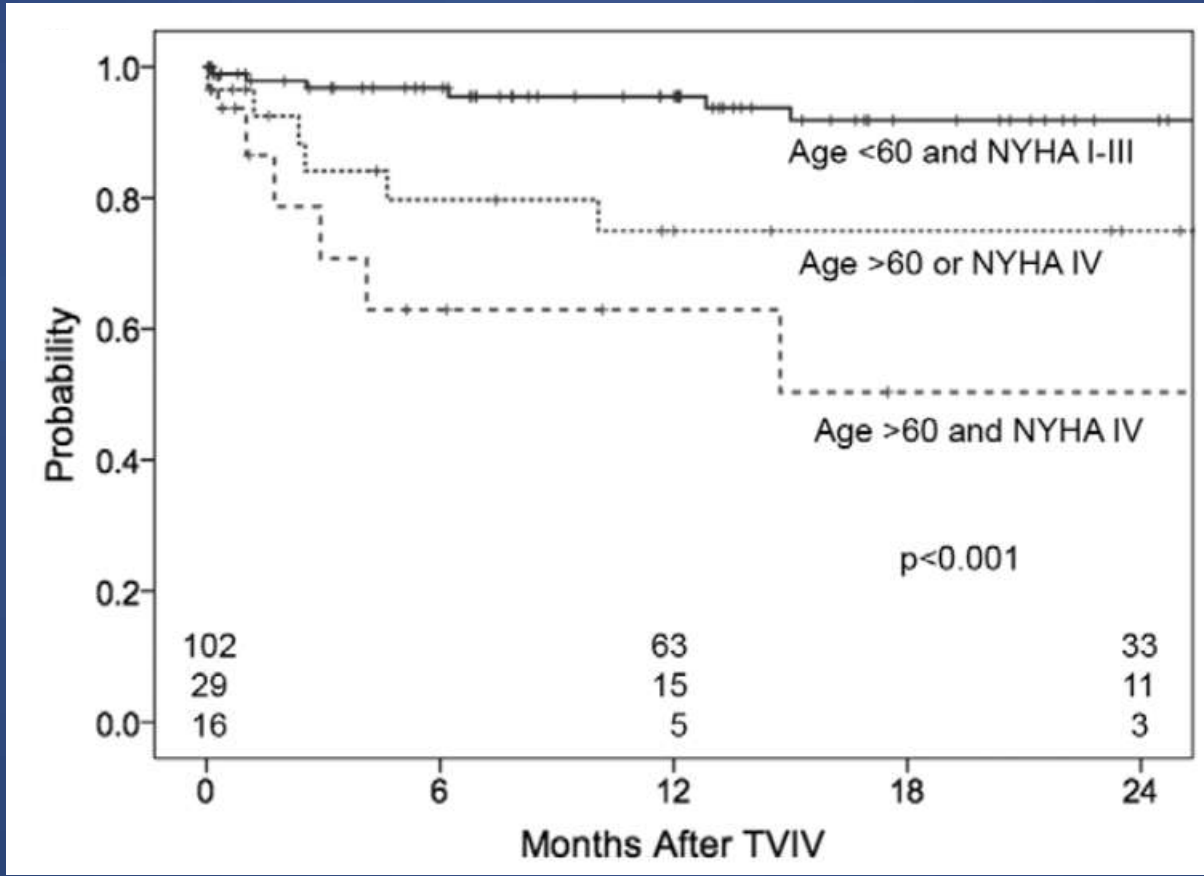
McElhinney D et al. Circulation. 2016;133:1582-1593.

Survival free from TVIV reintervention or significant TS (mean gradient ≥10) or TR



McElhinney D et al. Circulation. 2016;133:1582-1593.

VIVID Registry –TVIV
Survival after Tricuspid ViV



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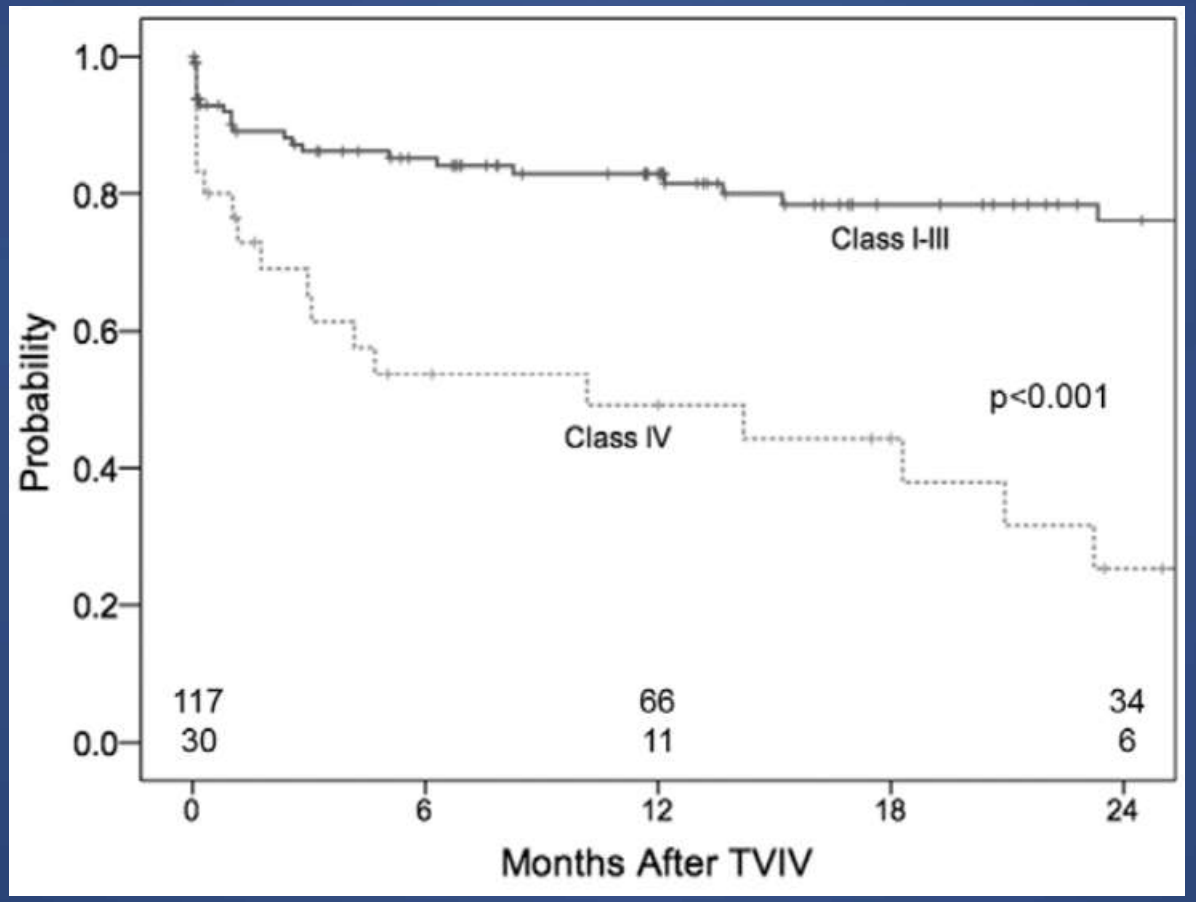


McElhinney D et al. Circulation. 2016;133:1582-1593.

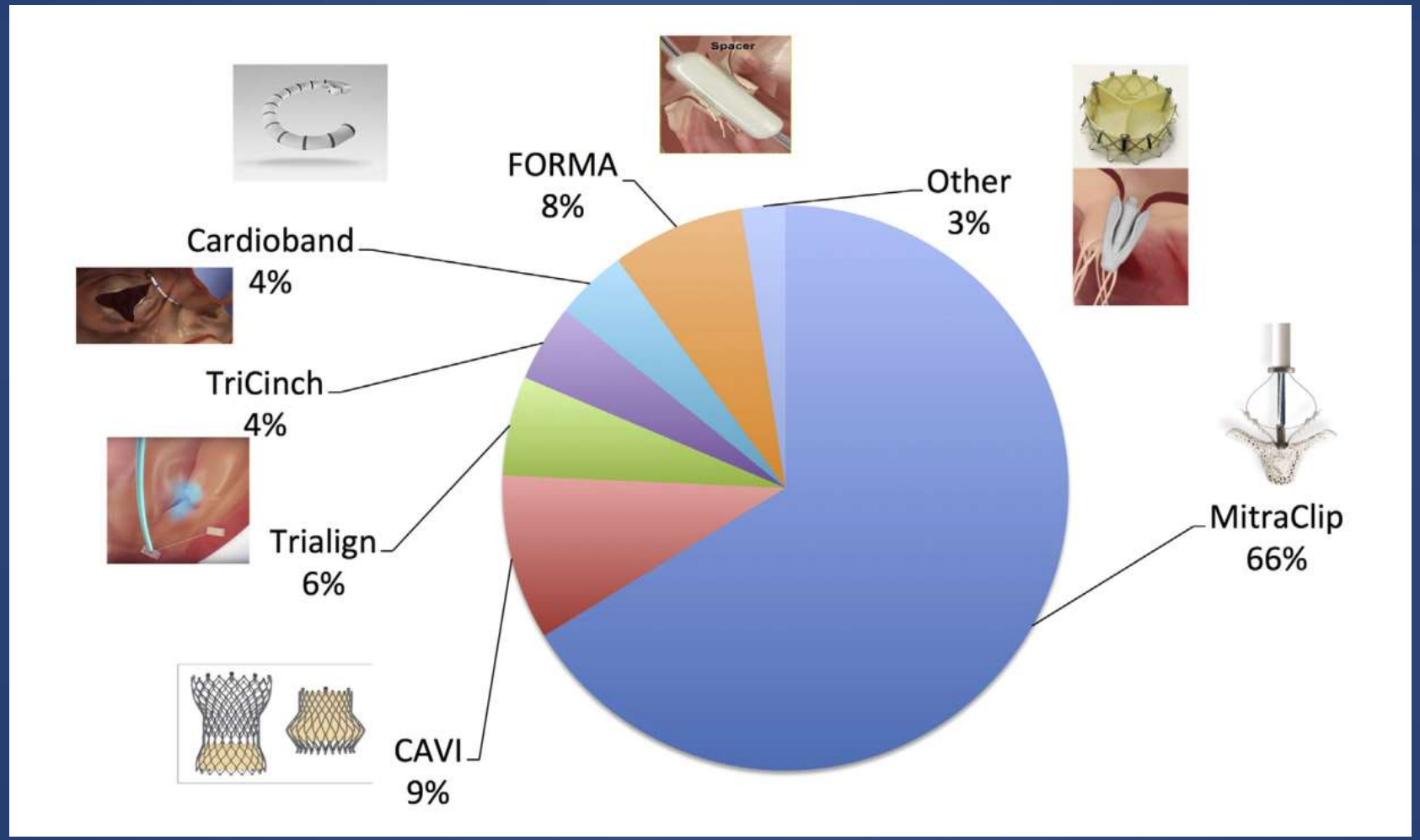
VIVID Registry –TVIV
Summary

- Tricuspid valve-in-valve procedures are increasingly performed using Melody and SAPIEN XT/ SAPIEN 3 THV devices.
- Although half the patients had etiology of congenital heart disease, most of them were adults at the time of VinV.
- Specific considerations in these cases include tx of large surgical valves, coaxilaity issues and transvalvular pacemaker leads.
- SAPIEN and Melody implantation for this indication show similar clinical outcomes.

Outcomes After Current Transcatheter TV Intervention

TriValve Registry – Mid-Term Results

312 high-risk patients with severe TR (93% of functional) at 18 centers



Taramasso M, et al. J Am Coll Cardiol Intv 2019;12:155–65

TriValve Registry
Patients' Clinical Characteristics

	N=312
Age (years)	76 ± 9
Female	171 (55)
EuroScore II	9 ± 8
Functional TR	288 (93)
Previous left side valve intervention (surgical/transcatheter/both)	84/24/3
Transvalvular tricuspid lead	71 (22)
NT pro-BNP, pg/mL	2759 (1298-5627)
Ascites	87 (28)
Peripheral oedema	265 (85)
NYHA functional class III-IV	297 (95)
Previous admission for RV failure	216 (69)

Values are n (%), mean (SD) or median (IQR)

Taramasso M, et al. J Am Coll Cardiol Intv 2019;12:155–65

TriValve Registry
Echocardiographic Characteristics

	N=312
Right atrial volume (ml)	111 ± 82
LV Ejection Fraction (%)	49 ± 13
Tricuspid Vena Contracta (cm)	1.1 ± 0.5
Tricuspid Regurgitant Volume (ml)	54 ± 34
Tricuspid Antero-Septal diameter (mm)	46.9 ± 9
Tricuspid EROA (mm2)	80 ± 60
TAPSE (mm)	16.2 ± 5
S-TDI (cm/sec)	10 ± 7
Coaptation Depth (mm)	9.5 ± 4.1
Tenting Area (cm2)	2.8 ± 1.7
Systolic Pulmonary Artery Pressure (mmHg)	41 ± 15

Values are mean (SD)

Taramasso M, et al. J Am Coll Cardiol Intv 2019;12:155–65

Echocardiographic Assessment of TR Severity

Current recommendations for grading the severity of chronic TR[1]

Parameters	Mild	Moderate	Severe
Structural			
TV morphology	Normal or mildly abnormal leaflets	Moderately abnormal leaflets	Severe valve lesions
RV and RA size	Usually normal	Normal or mild dilatation	Usually dilated
IVC diameter	Normal < 2 cm	Normal or mildly dilated 2.1-2.5 cm	Dilated > 2.5 cm
Qualitative			
Color flow jet area	Small, narrow, central	Moderate central	Large central jet or eccentric wall-impinging jet
Flow convergence zone	Not visible, transient or small	Intermediate	Large throughout systole
CWD jet	Faint/partial/parabolic	Dense, parabolic or triangular	Dense, often triangular
Semi-quantitative			
Color flow jet area (cm^2)	Not defined	Not defined	>10
VCW (cm)	<0.3	0.3-0.69	≥0.7
PISA radius (cm)	≤0.5	0.6-0.9	>0.9
Hepatic vein flow	Systolic dominance	Systolic blunting	Systolic flow reversal
Tricuspid inflow	A-wave dominant	Variable	E-wave >1.0 m/sec
Quantitative			
EROA (mm^2)	<20	20-39	≥ 40
RVol (2D PISA) (mL)	<30	30-44	≥45

Proposed extended grading scheme[2]

Variable	Mild	Moderate	Severe	Massive	Torrential
VC (biplane) (mm)	< 3	3-6.9	7-13	14-20	≥ 21
EROA (PISA)(mm^2)	< 20	20-39	40-59	60-79	≥ 80
3D VCA or quantitative EROA(mm^2)			75-94	95-114	≥ 115

[1]Zoghbi et al. *JASE* 2017
[2]Hahn RT and Zamorano JL. *EHJ-CVI* 2017

TriValve Registry
Procedural and 30-day outcomes

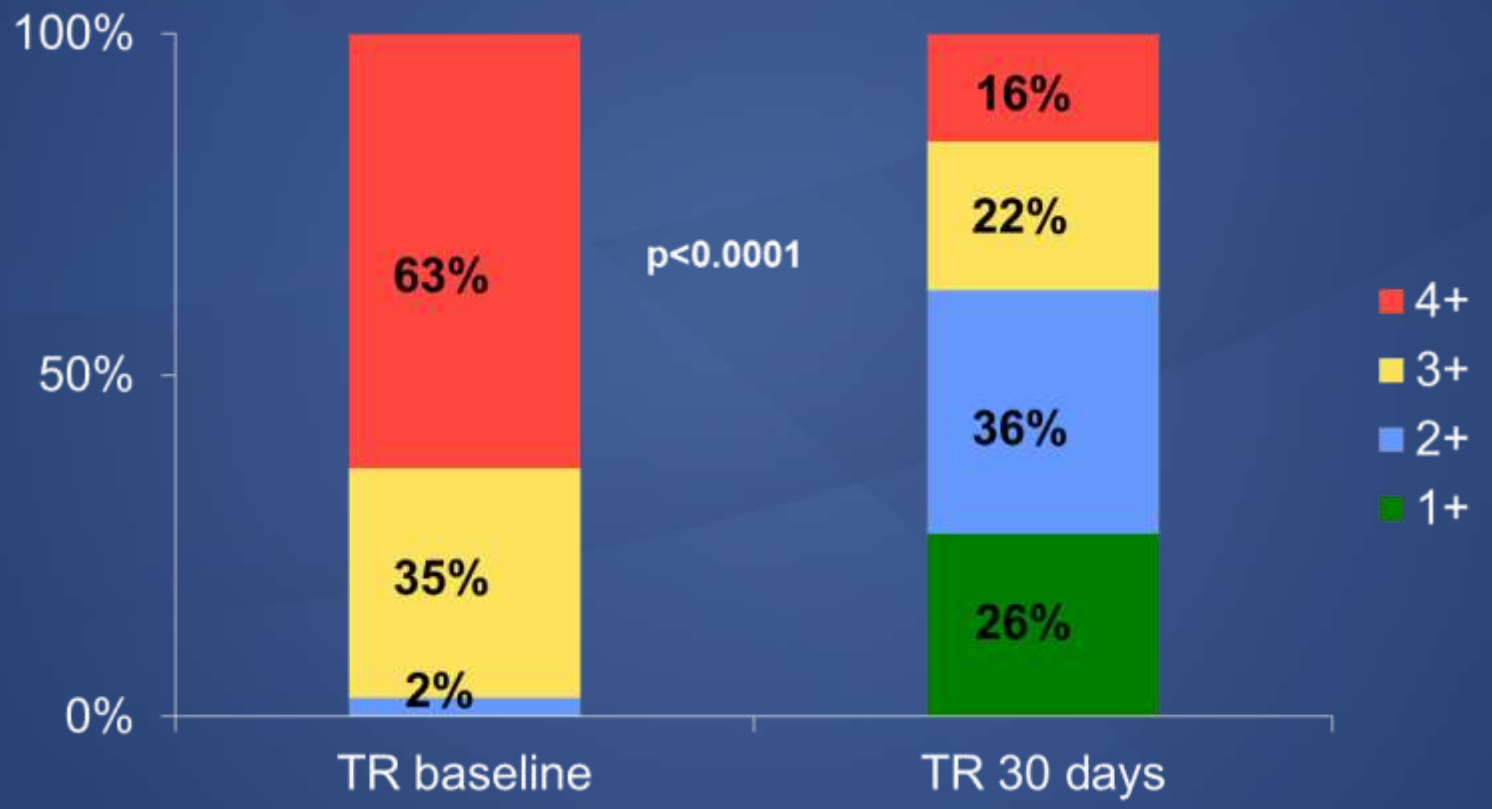
	N=280
Procedural Success	204 (72.8)
Thirty-day Mortality	10 (3.6)
Major bleeding	5 (1.7)
Stroke	3 (1.0)
Myocardial infarction requiring right coronary artery stenting	2 (0.7)
Conversion to surgery	4 (1.4)
Respiratory failure	2 (0.7)
Device detachment	1 (0.3)
Ventricular arrhythmia	1 (0.3)

Values are n (%)

Taramasso M, et al. J Am Coll Cardiol Intv 2019;12:155–65

Transcatheter Therapies for TR

Reduction in TR Severity



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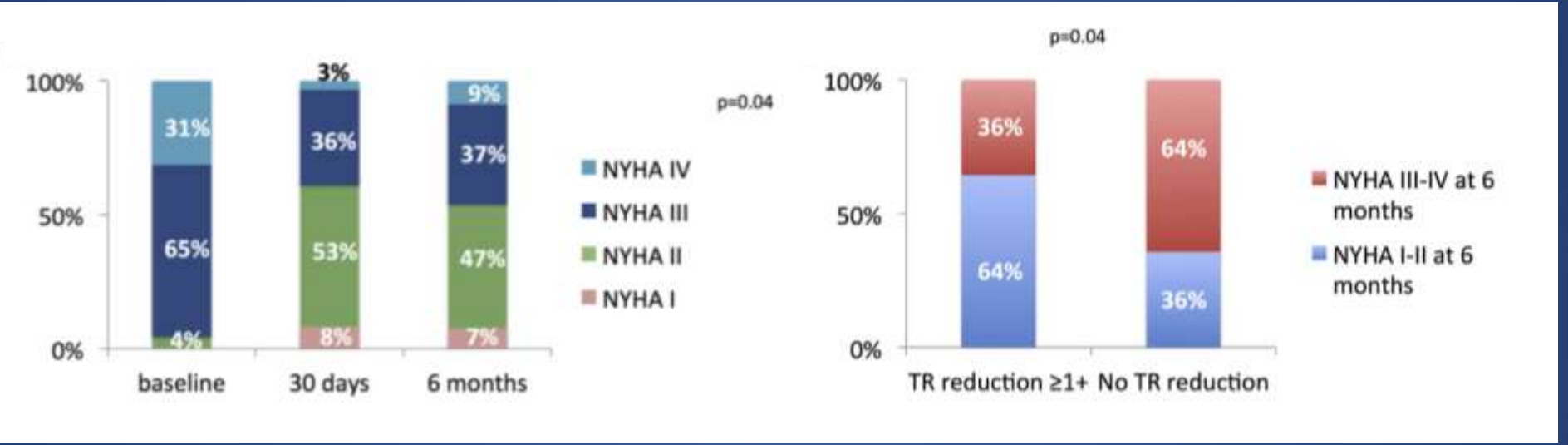
Transcatheter Therapies for TR
Changes in Functional Status



- Patients with ascites: from 27% → 14% (p=0.006)
- Patients with peripheral oedema: from 89% to 39% (p=0.001)

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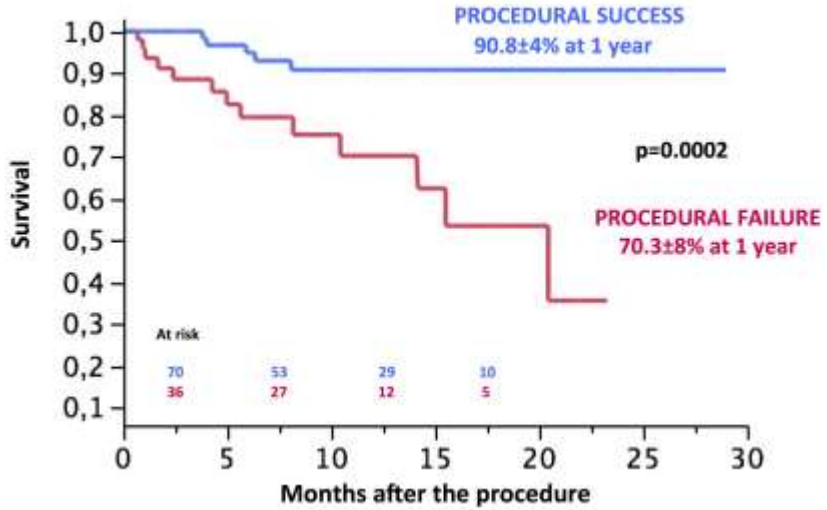
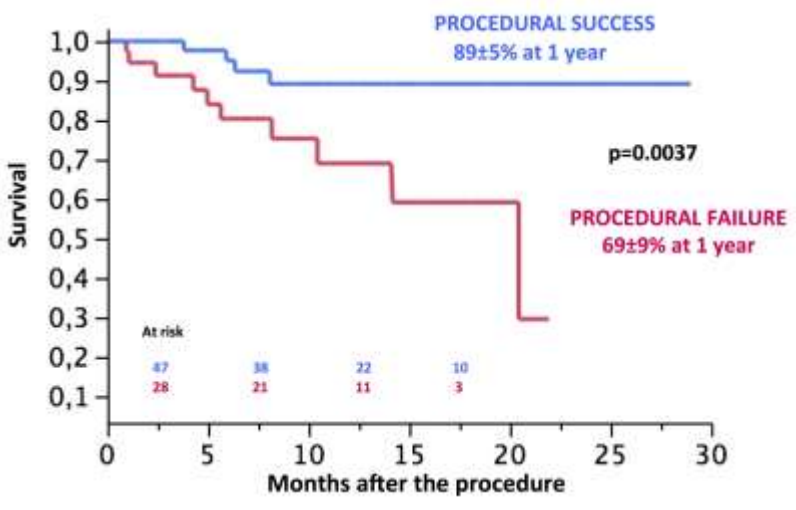
TriValve Registry
Follow-up

Overall Survival according to Procedural Success



Survival Isolated TTVI according to Procedural Success



Procedural success and higher values of sPAP at baseline were independently associated with increased mortality at follow-up

TriValve Registry
Summary

- Procedural success, defined as successful device implantation and residual TR of ≤ 2+, achieved in 72.8%
- At a median follow-up of 6 months, improvements seen in NYHA class and prevalence of ascites and peripheral edema
- At 1.5 years, the actuarial survival rate was 77.2 ± 5.9%
- Procedural success (HR 0.18) and systolic pulmonary artery pressure (HR 17.0) independently predicted mortality

TriValve Registry
Conclusions

- Several challenges in TTVI (anatomy, imaging, clinical, definitions)
- TTVI is feasible with different technologies, with a reasonable overall procedural success rate and it is associated with low mortality and significant clinical improvement
- Mid-term survival is “favorable” in this high risk population
- Patient selection is crucial (anatomical and clinical)

Ongoing and Future Studies on TTVI

Ongoing studies on transcatheter therapies for tricuspid regurgitation for each devices.

Device	Name (NCT)	Design	N° patients	TR severity	Surgical risk	Primary outcome
TriClip	TRILUMINATE (NCT03904147)	Randomized, open-label	700	Severe or more	Intermediate or more	Hierarchical composite of all-cause mortality or tricuspid valve surgery, rate of heart failure hospitalizations, and quality of life improvement at 12 months
PASCAL	CLASP II TR (NCT04097145)	Randomized, open-label	825	Severe or more	Intermediate ore more	Hierarchical composite of adverse events including mortality, heart failure hospitalisation, need for tricuspid valve surgery, and improvement of quality of life at 24 months
MISTRAL	MATTERS II (NCT04073979)	First-in-man Prospective registry	10	Moderate or more	High risk	Acute safety with rate of device related serious adverse events at procedure, 5 and 30 days
Trialign	SCOUT II (NCT03225612)	Prospective registry	60	Moderate or more	High risk	All-cause mortality at 30 days
MIA	STTAR (NCT03692598)	Prospective registry with parallel arms (surgical and percutaneous)	60	Moderate or more	Excluded if unacceptable surgical risk	Safety: Major adverse events within 30 days of the procedure including death, cardiac tamponade, MI, cardiac surgery for failed MIA implantation, or stroke Efficacy: Reduction in tricuspid regurgitation at 30 days
Cardioband	TriBAND (NCT03779490)	Prospective post-market registry	150	Moderate or more	–	Reduction in severity of Tricuspid Regurgitation at discharge.
DaVingi	NCT03700918	First-in-human prospective registry	15	Severe or more	–	Safety: device-related serious adverse at 30 days Efficacy: Rate of successful adjustment of the DaVingi ring
TricValve	TRICUS STUDY (NCT03723239)	Prospective registry	10	n/a	–	Safety: Percentage of participants with major adverse events at 30 days Efficacy: Change of (NYHA) functional class at 6 months
	TRISCEND (NCT04221490)	Early feasibility prospective registry	200	Moderate or more	–	Freedom from device or procedure-related adverse events at 30 days
Evoque	TRISCEND II (NCT04482062)	Randomized, open-label	775	Severe or more	–	- TR grade reduction and composite of functional endpoint including: Kansas city cardiomyopathy questionnaire, NYHA functional class, and 6-minute walk test distance improvement at 6 months - Rate of Major adverse events at 30 days - Composite endpoint including all-cause mortality, right ventricle assistance device implantation or heart transplant, tricuspid valve intervention, heart failure hospitalizations, and functional improvement at 1 year
LuX-Valve	TRAVEL (NCT04436653)	Prospective registry	150	Severe or more	High risk	All-cause death at 1 year. Tricuspid regurgitation reduction at 1 year
Cardiovalve	NCT04100720	Early feasibility prospective registry	15	Moderate or more	–	Safety: Patients free of major adverse events at 30 days Efficacy: technical success and tricuspid regurgitation reduction at 30 days

NYHA: New York Heart Association, TR: tricuspid regurgitation.

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