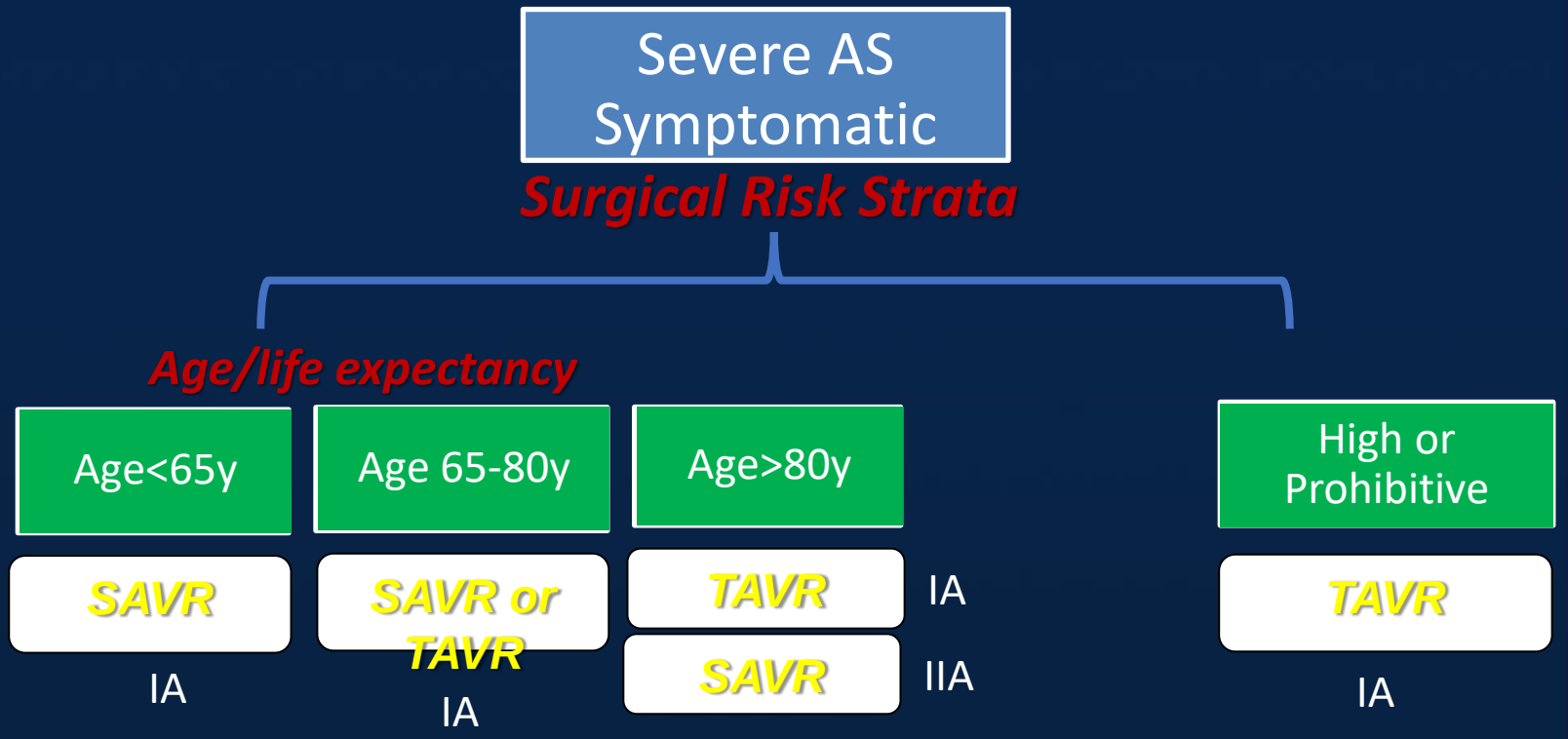
# TAVR

## Transcatheter Aortic Valve Replacement

# ACC/AHA TAVR Guidelines 2020

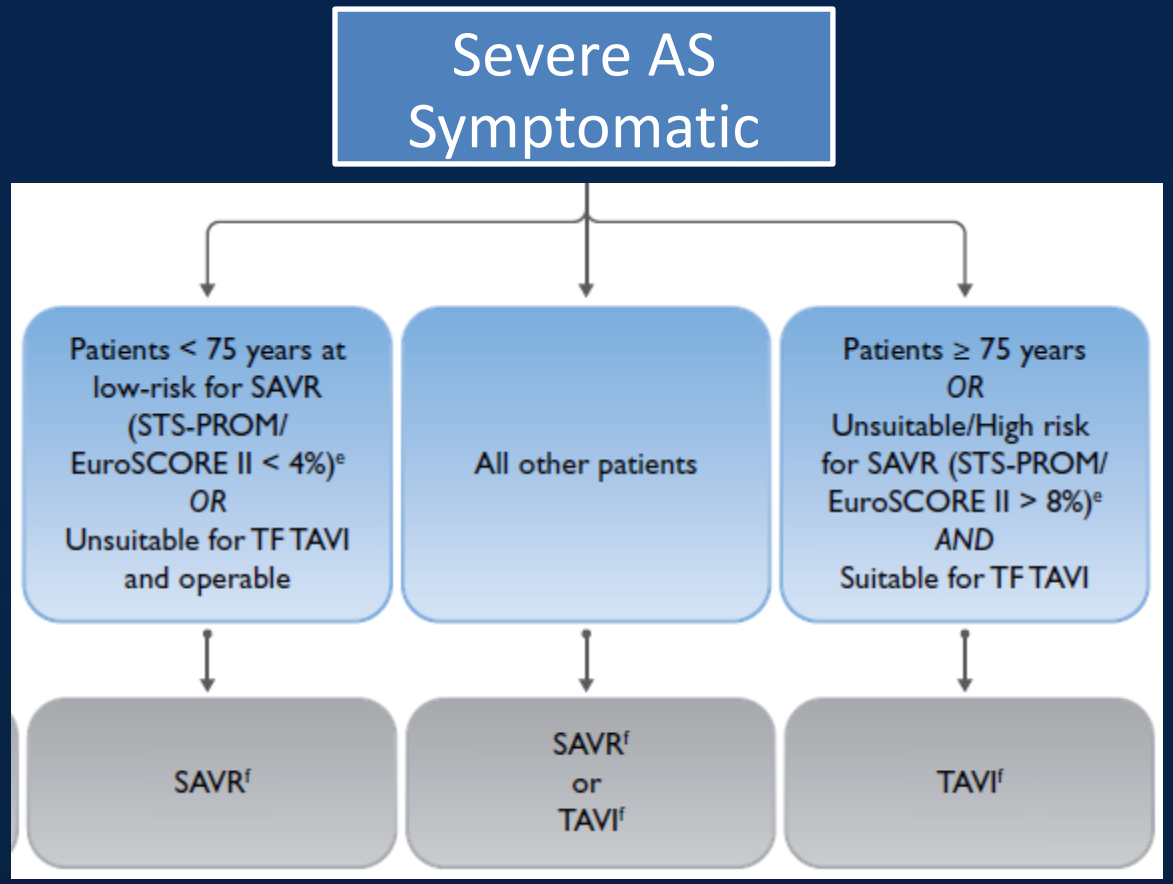
## 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease

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

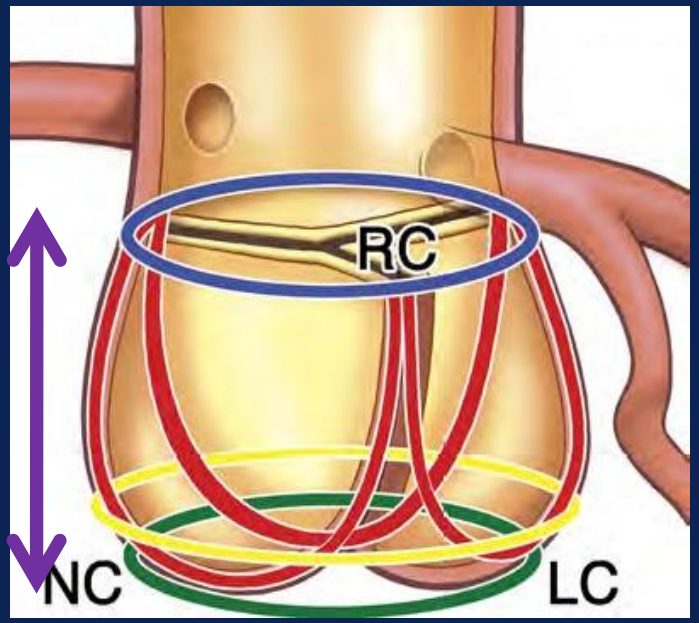


# ESC TAVR Guidelines 2021

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



# Aortic Root Anatomy




Sinotubular junction

Aortic leaflets

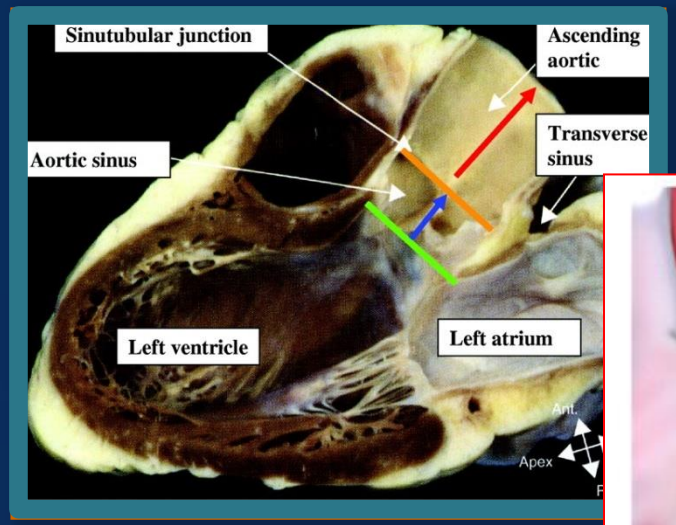
Aortic Annulus

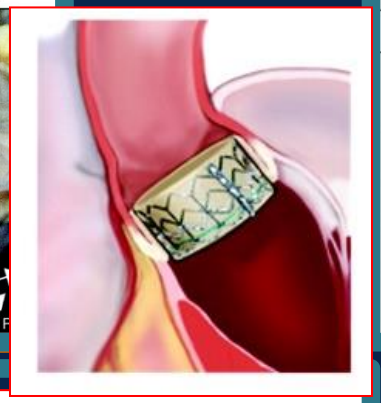
AVA-coronary height

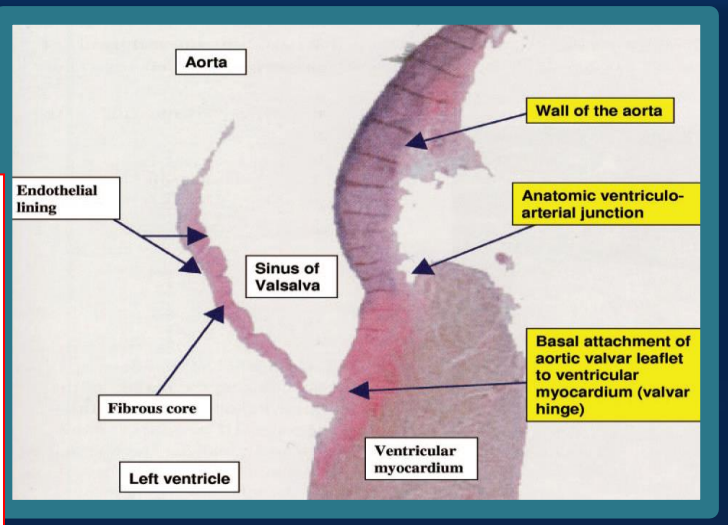
RC = Right coronary cusp; NC = Non-coronary cusp; LC = Left coronary cusp

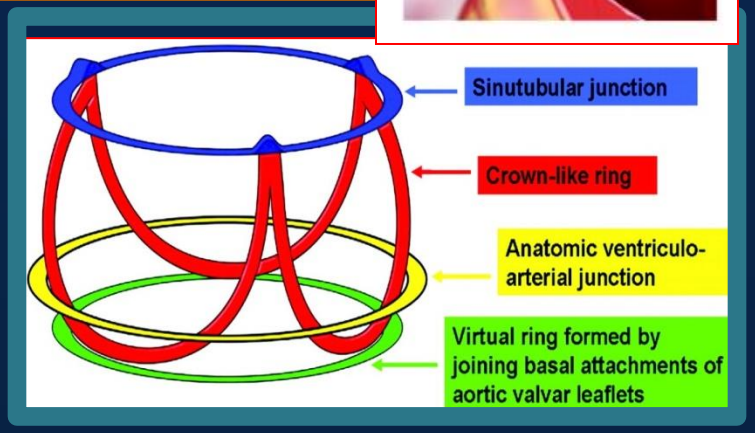
Valve size should be based on the largest diameter of the AV annulus

# Anatomy of Aortic Valvular Complex





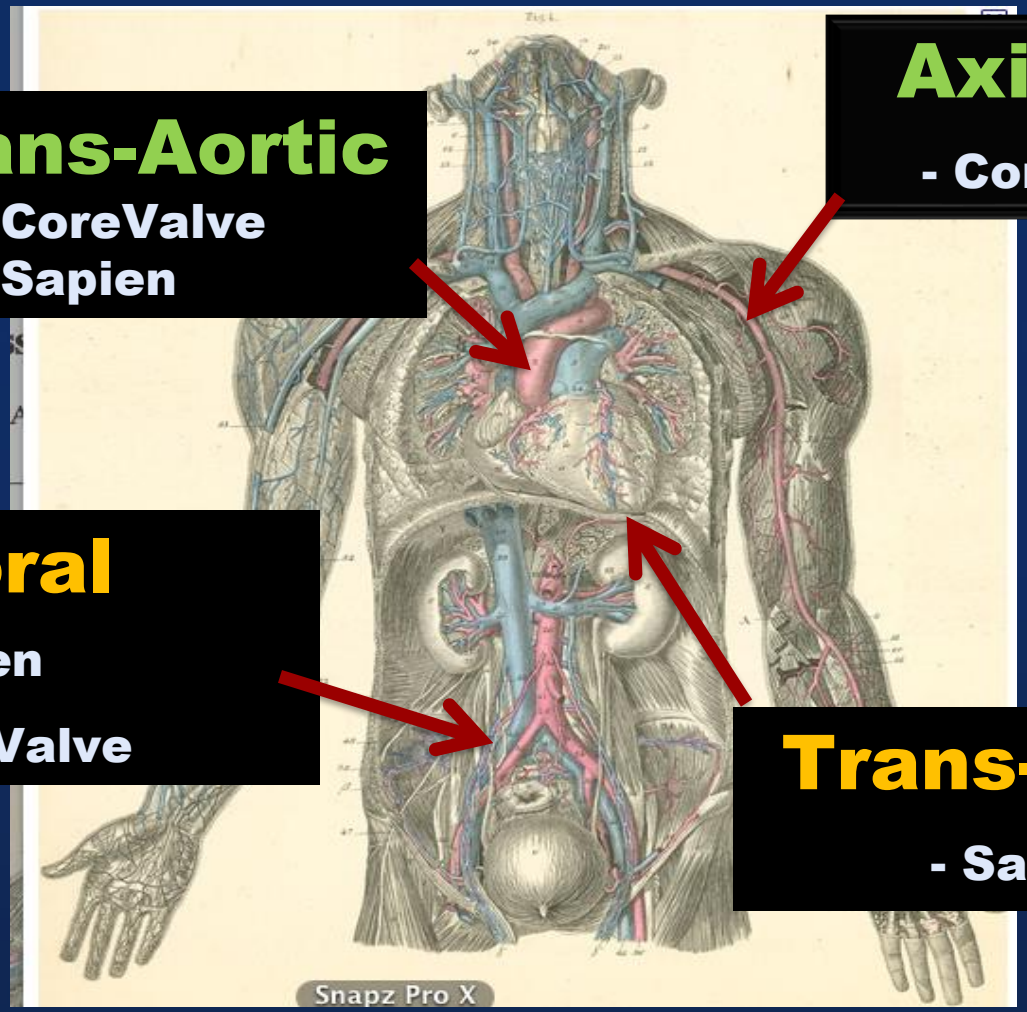




***Stability of valve probably determined by the "virtual ring"***

***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



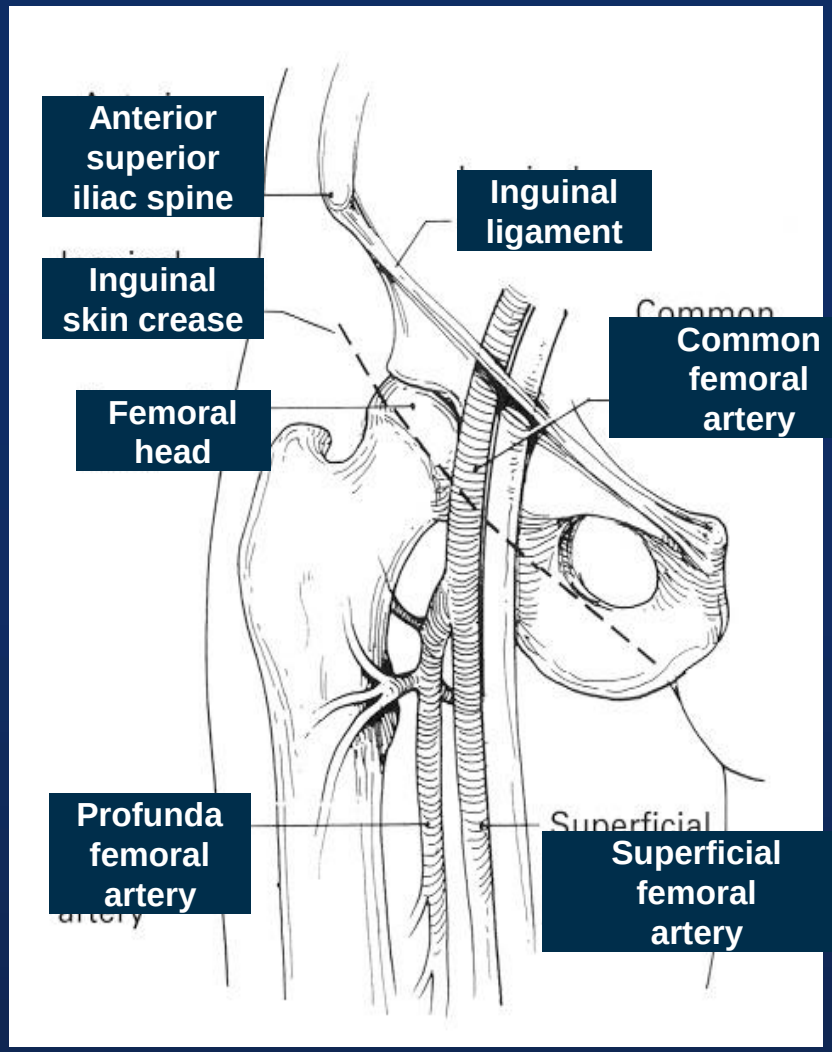

**Trans-Aortic**
- CoreValve
- Sapien

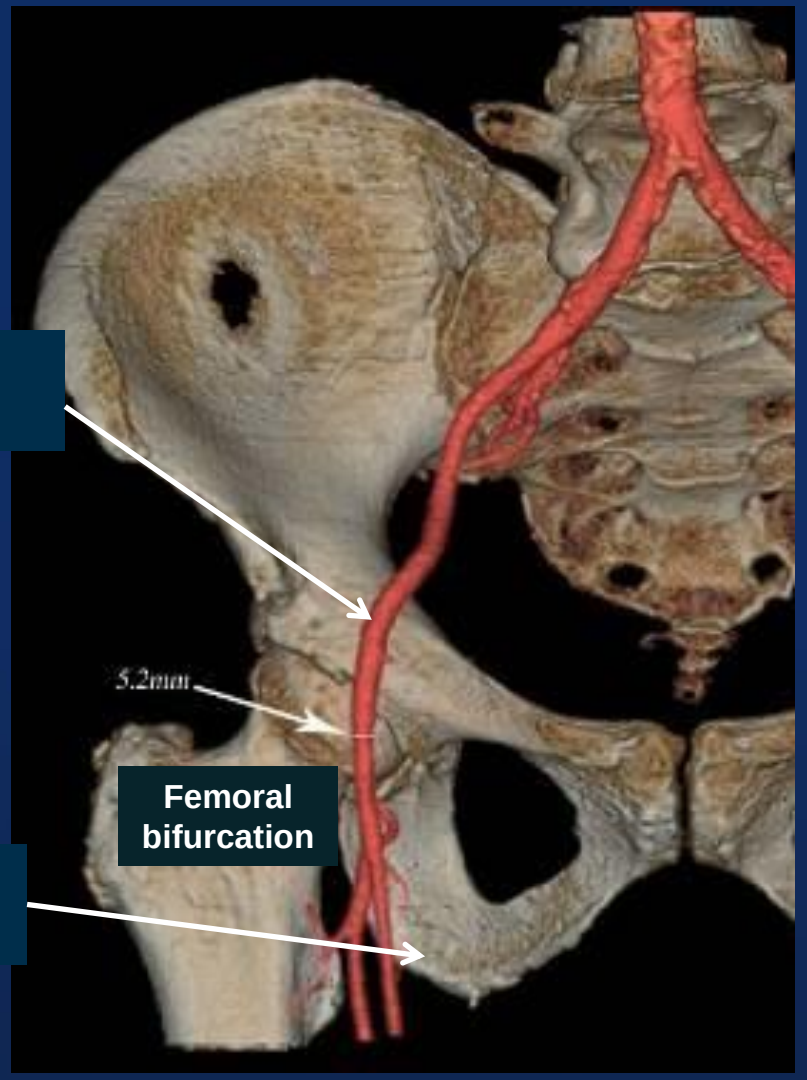
**Axillary**
- CoreValve

**Femoral**
- Sapien
- CoreValve

**Trans-apical**
- Sapien

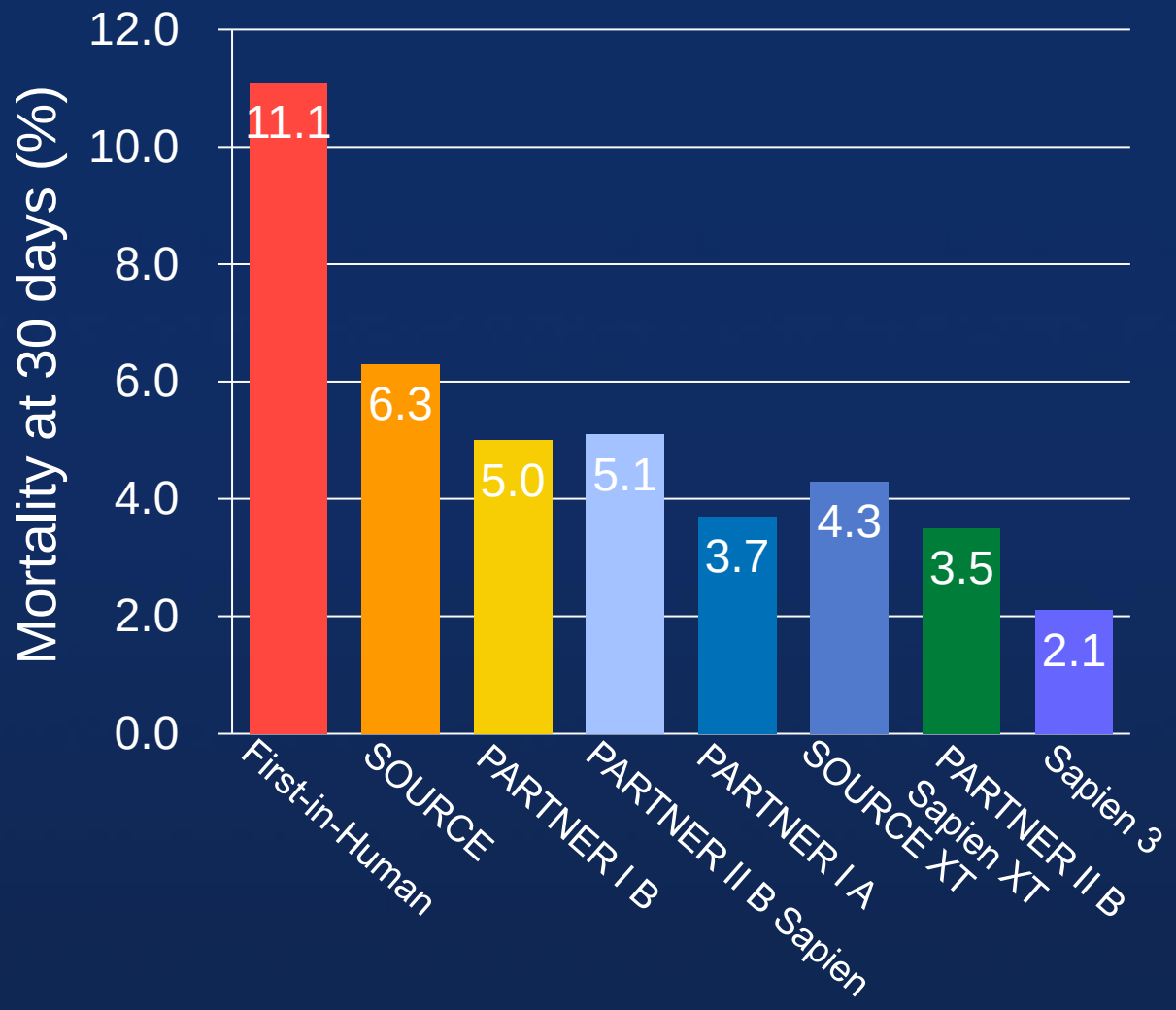
# Femoral Artery Anatomy



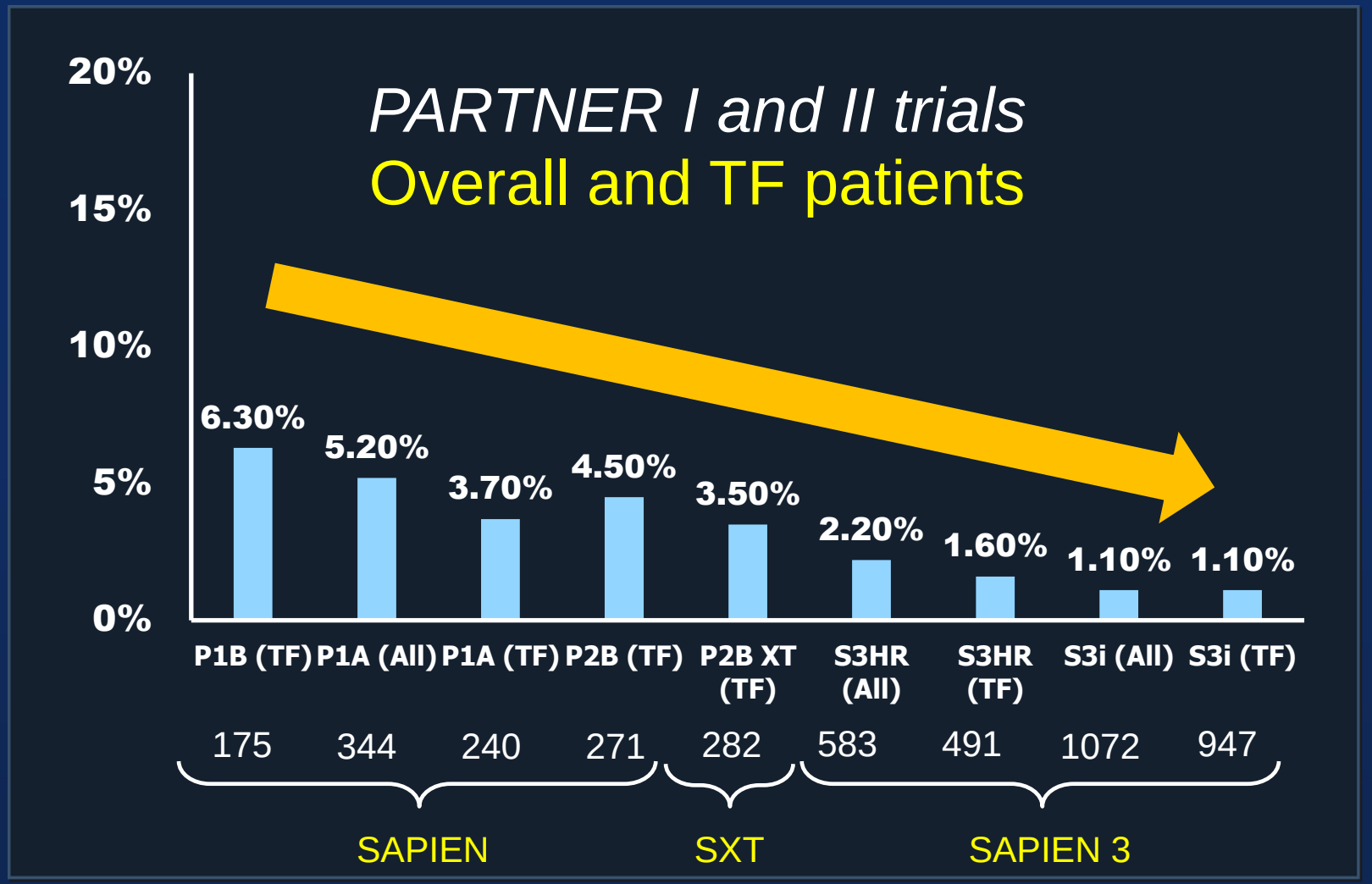
# Trend of TAVR

# Mortality Across TAVR Studies

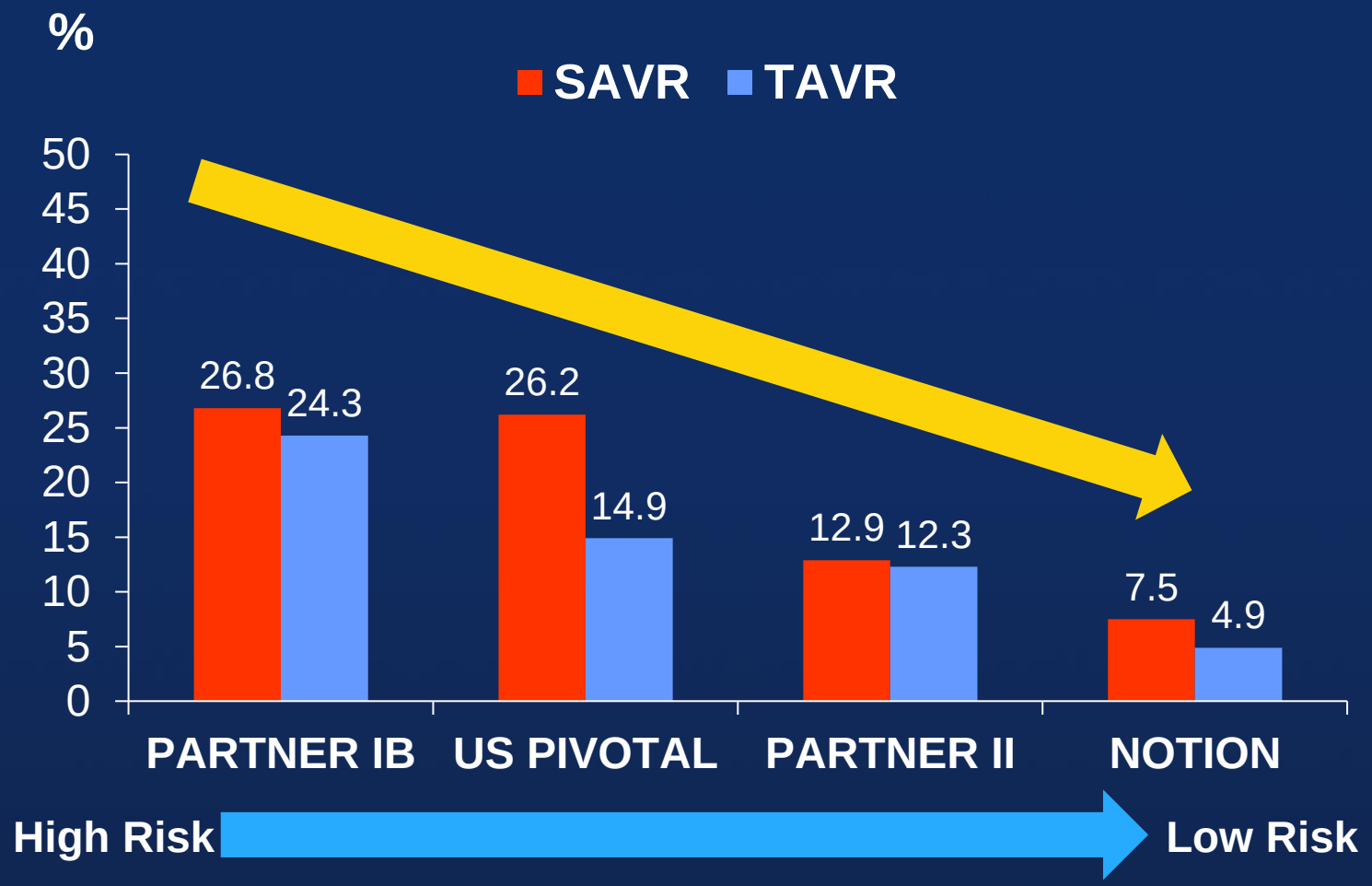


# All-Cause Mortality at 30 Days

## Edwards SAPIEN Valves



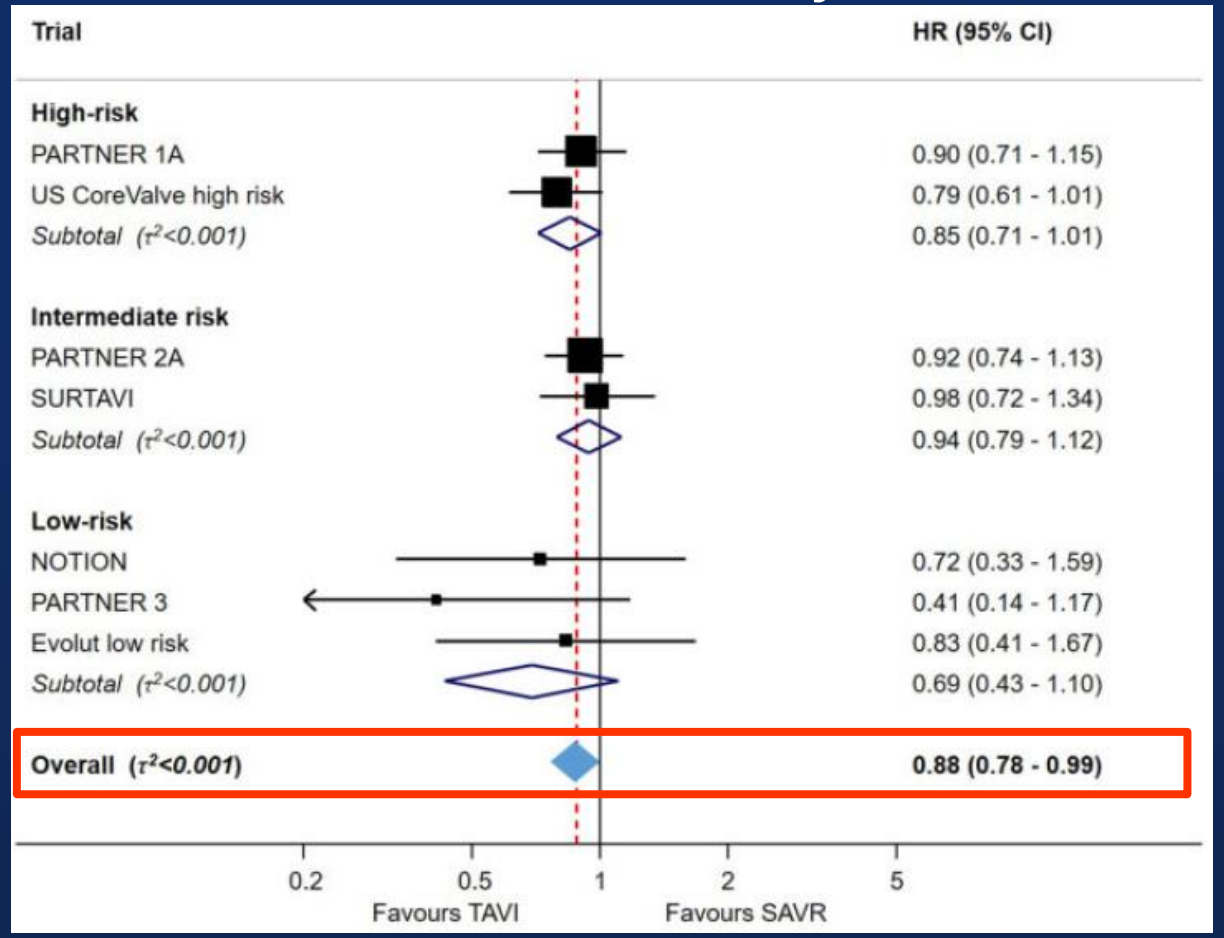
# All Cause Mortality @ 1 Year



# Metaanalysis From Randomized Trials

## Survival Benefit In TAVR

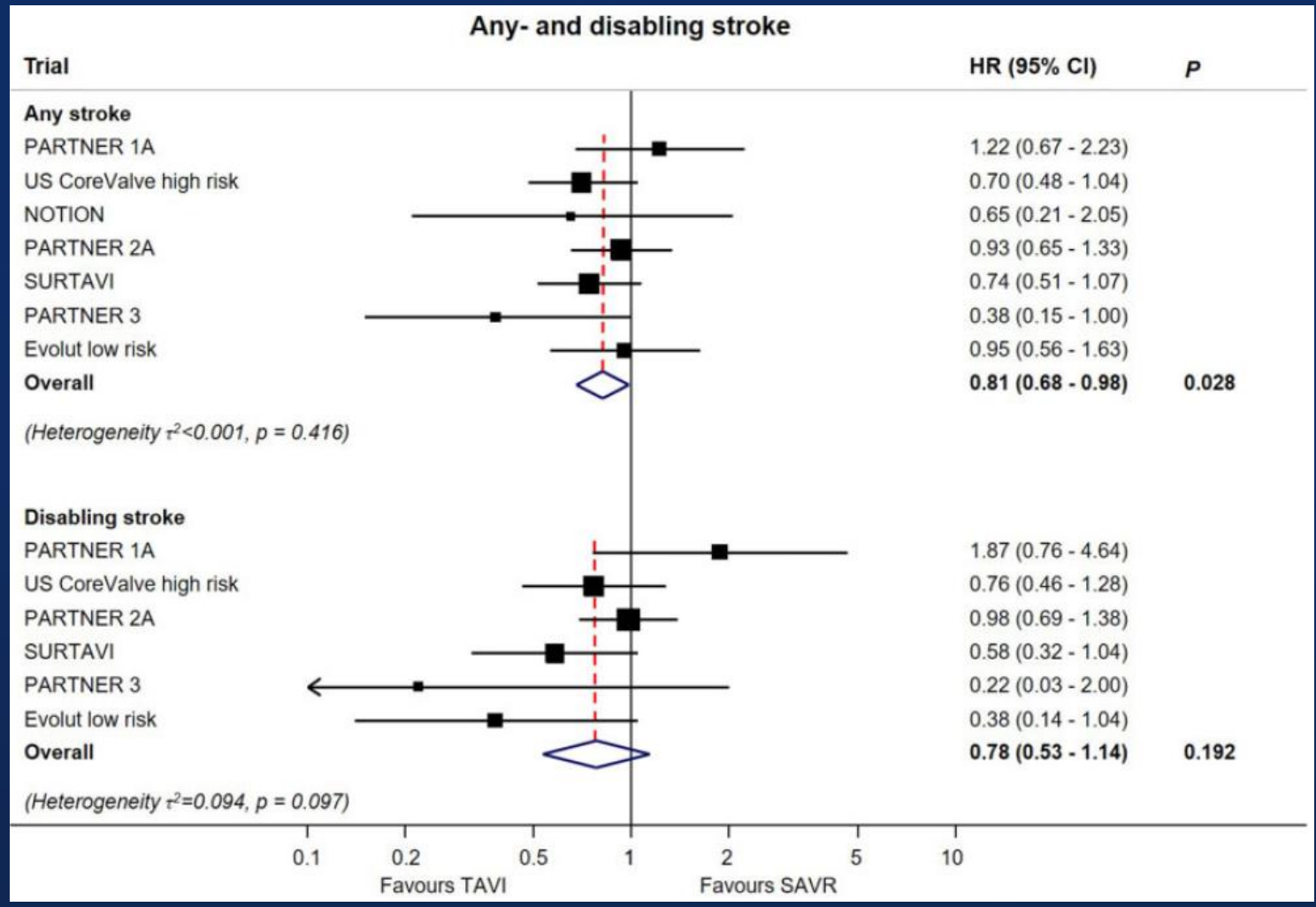
### All-cause mortality






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

# Metaanalysis From Randomized Trials

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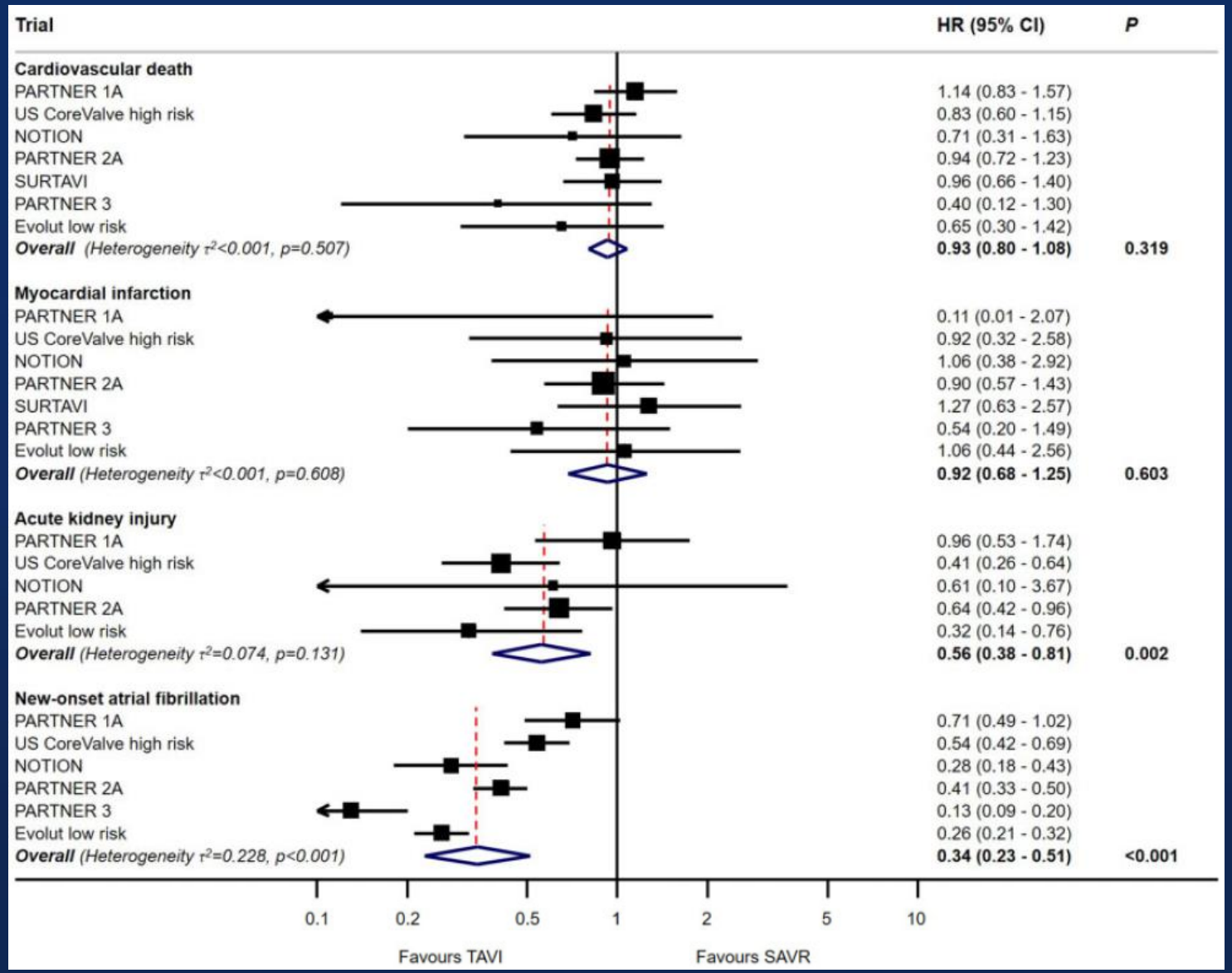
# Metaanalysis From Randomized Trials

## Analyses for the secondary outcomes

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# Metaanalysis From Randomized Trials

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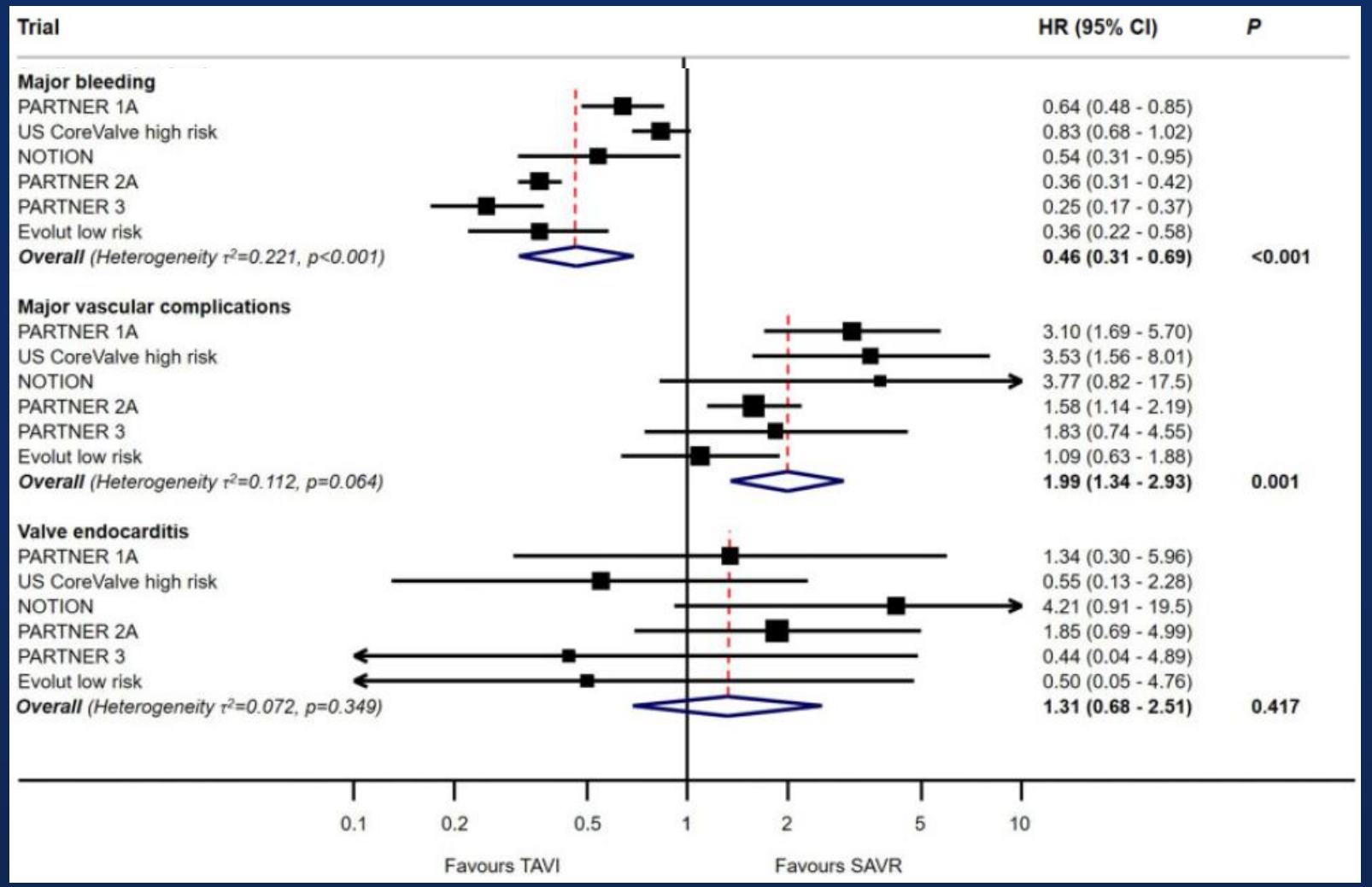





Siontis GC et al Eur Heart J European Heart Journal (2019) 40, 3143–3153

# *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

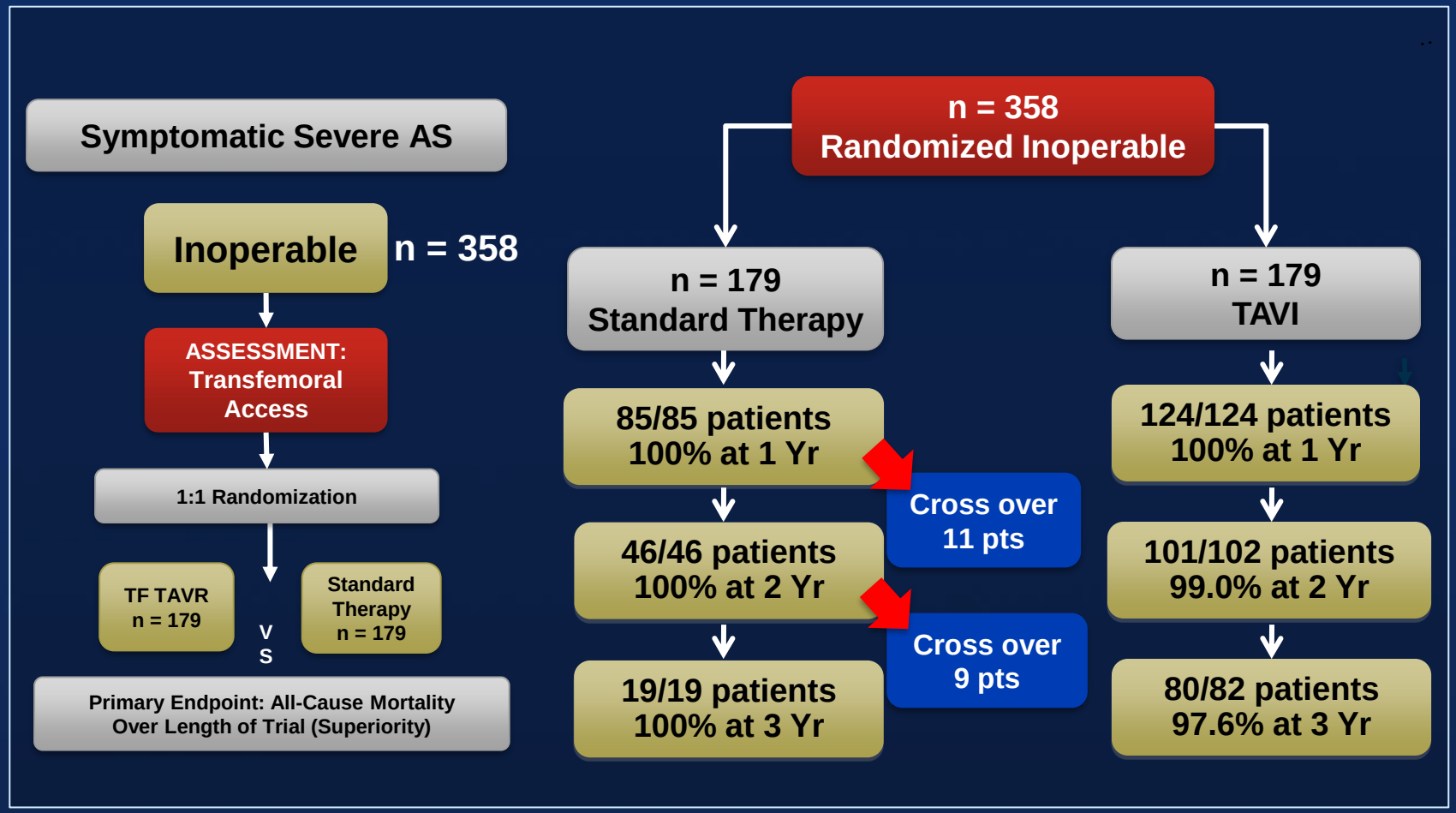
# Edwards SAPIEN
# balloon-expandable THV

# SAPIEN valve trials

## PARTNER trial

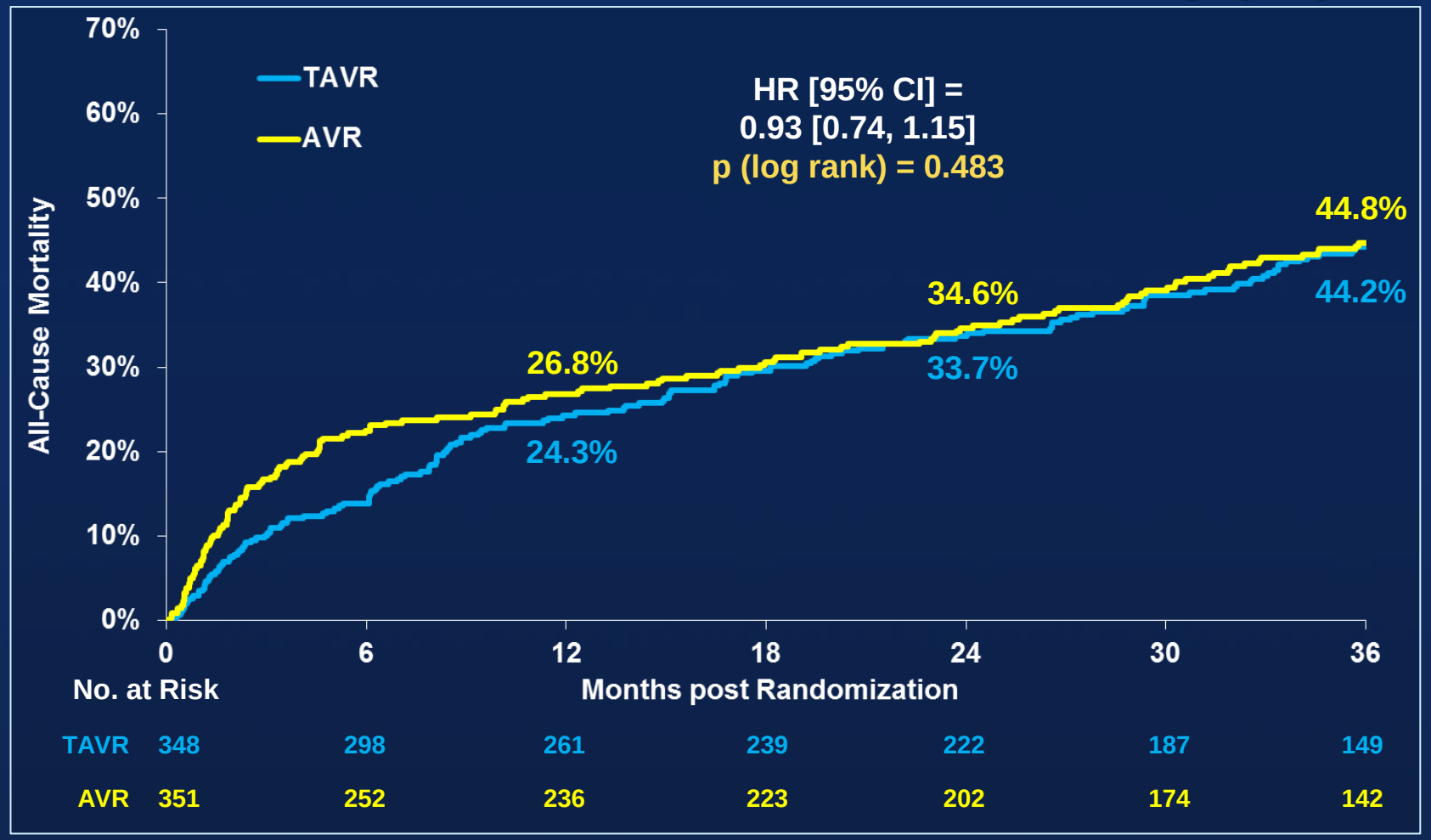
# PARTNER trial : Inoperable

## 3 year follow-up



# PARTNER trial : High Risk

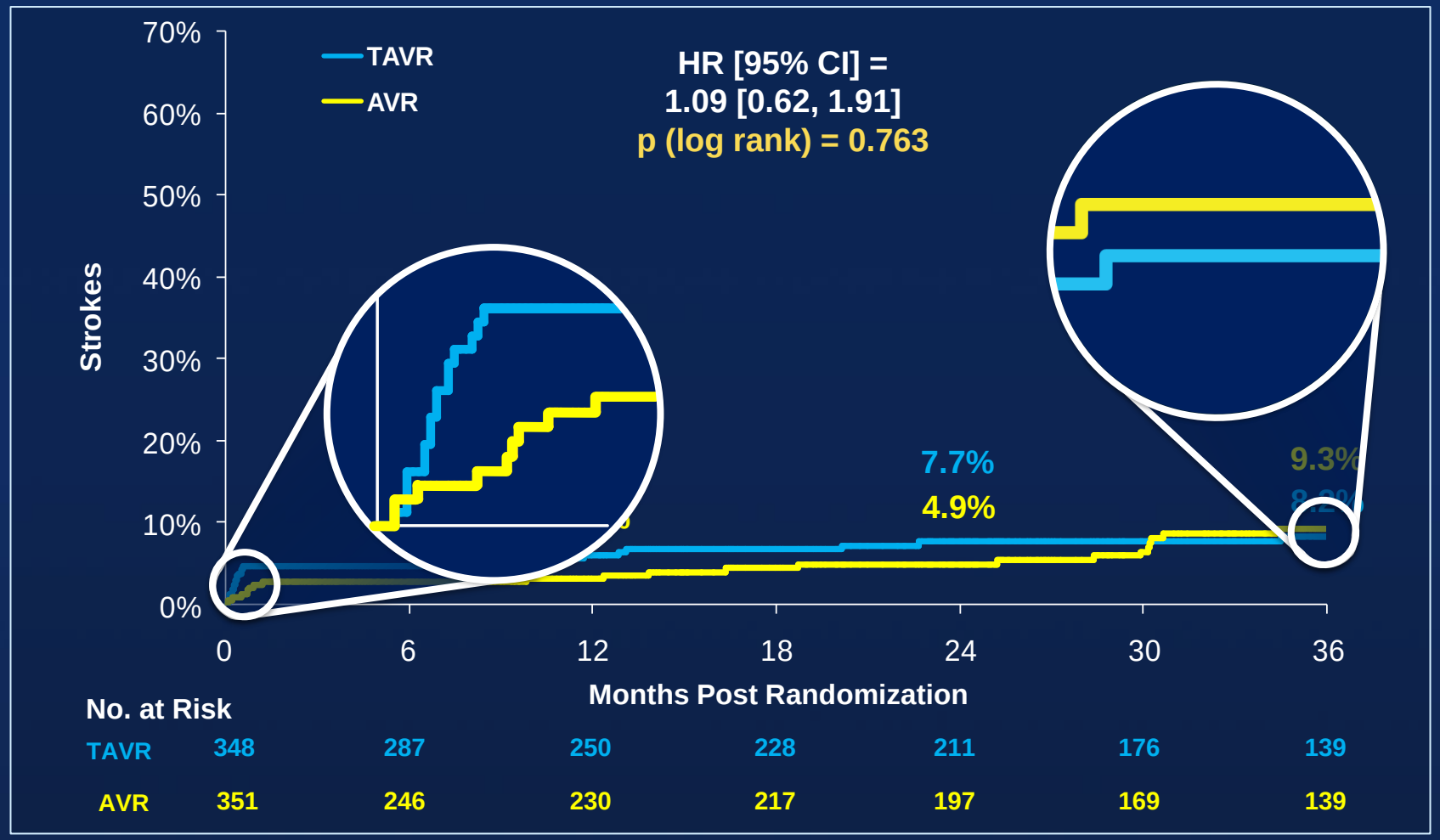
## 3 year follow-up All-Cause Mortality (IIT)




Vinod H. Thourani et al. ACC 2013

# PARTNER trial : High Risk

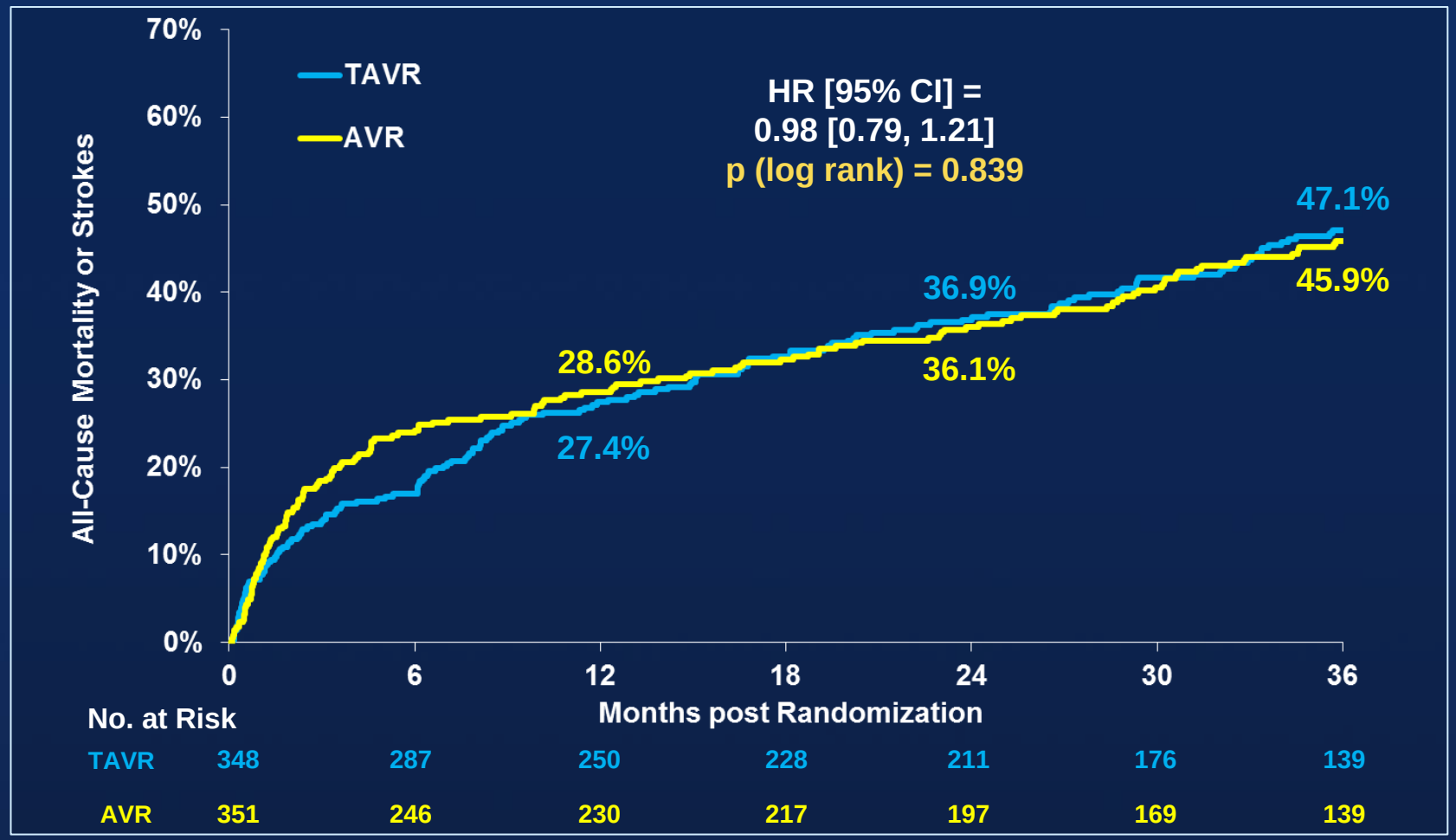
## 3 year follow-up Stroke (IIT)




Vinod H. Thourani et al. ACC 2013

# PARTNER trial : High Risk

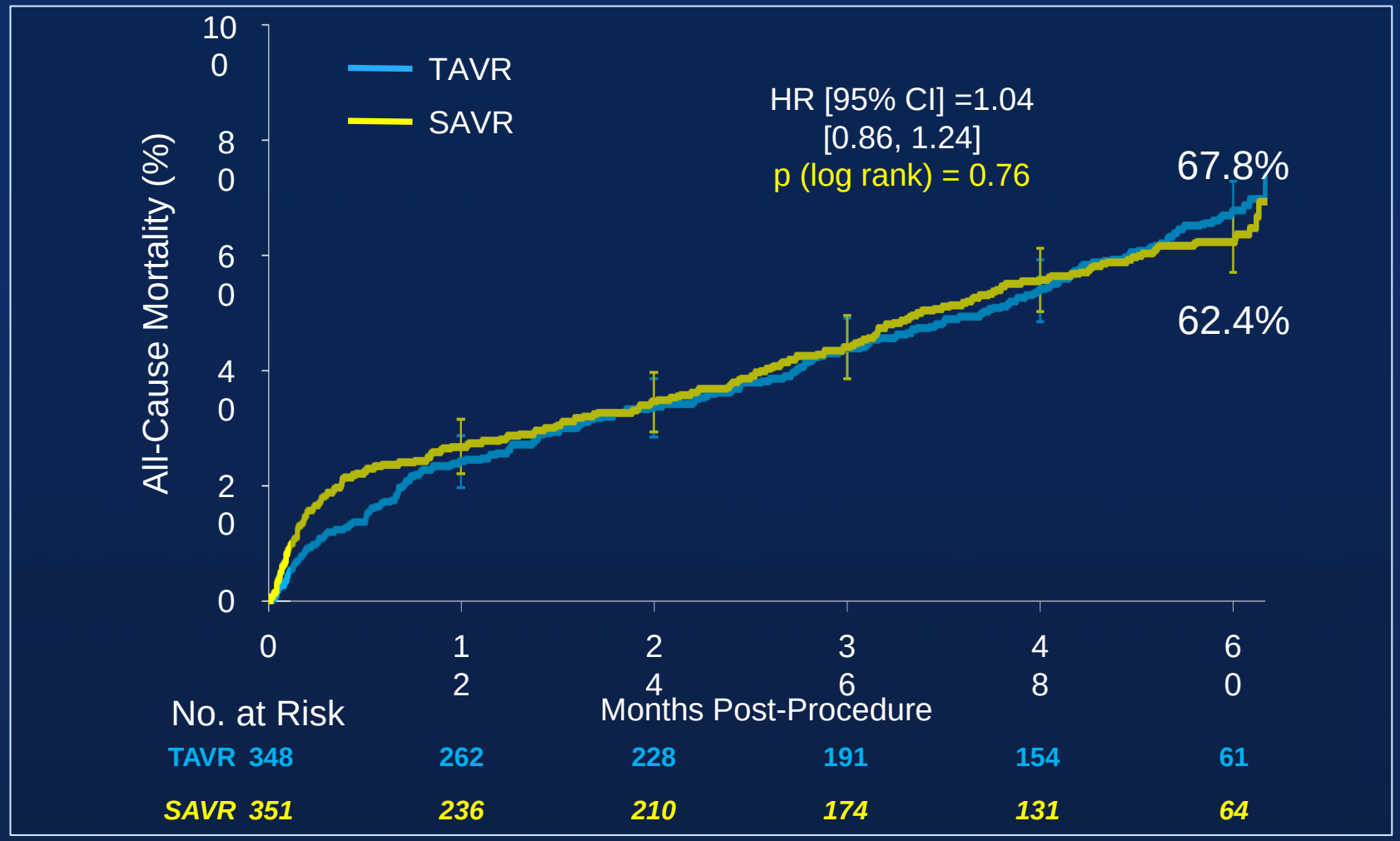
## 3 year follow-up All-Cause Mortality or Strokes (IIT)




Vinod H. Thourani et al. ACC 2013

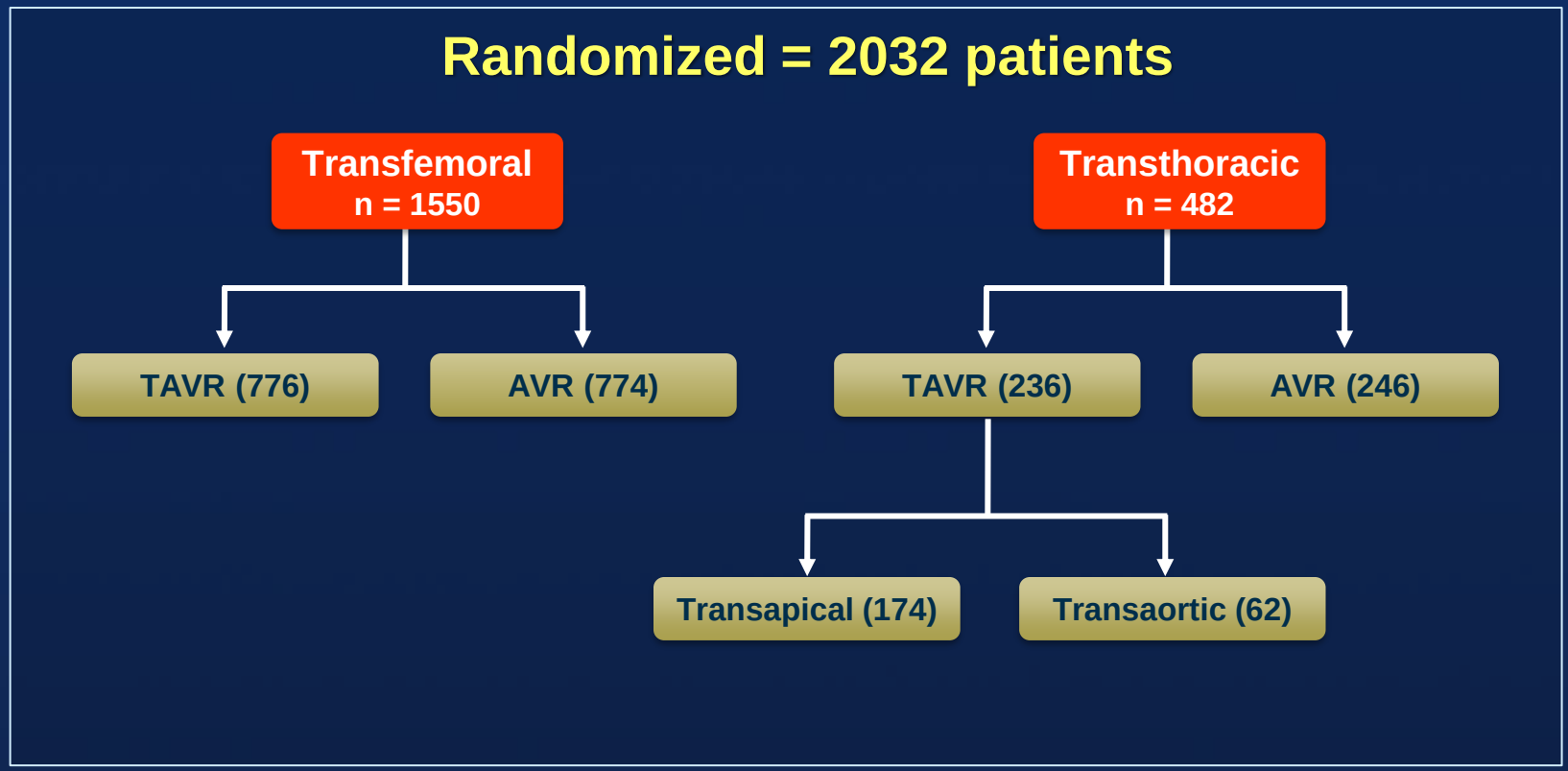
# 5 Years Outcomes of PARTNER I trial

## All-Cause Mortality (ITT)



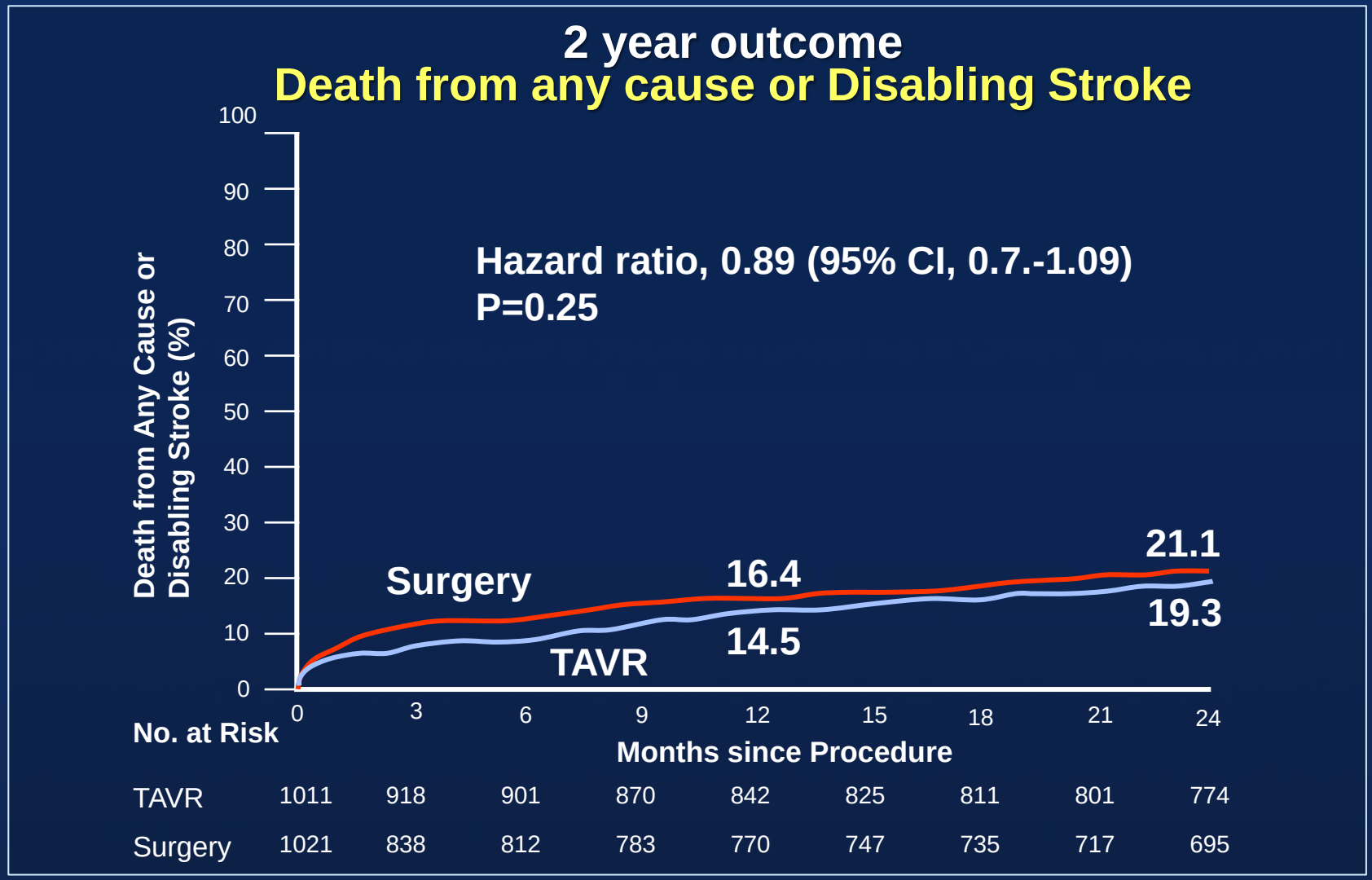
# PARTNER 2 trial Cohort A

## TAVR (SAPIEN XT) VS AVR
## Intermediate risk




Martin B. Leon et al NEJM 2016

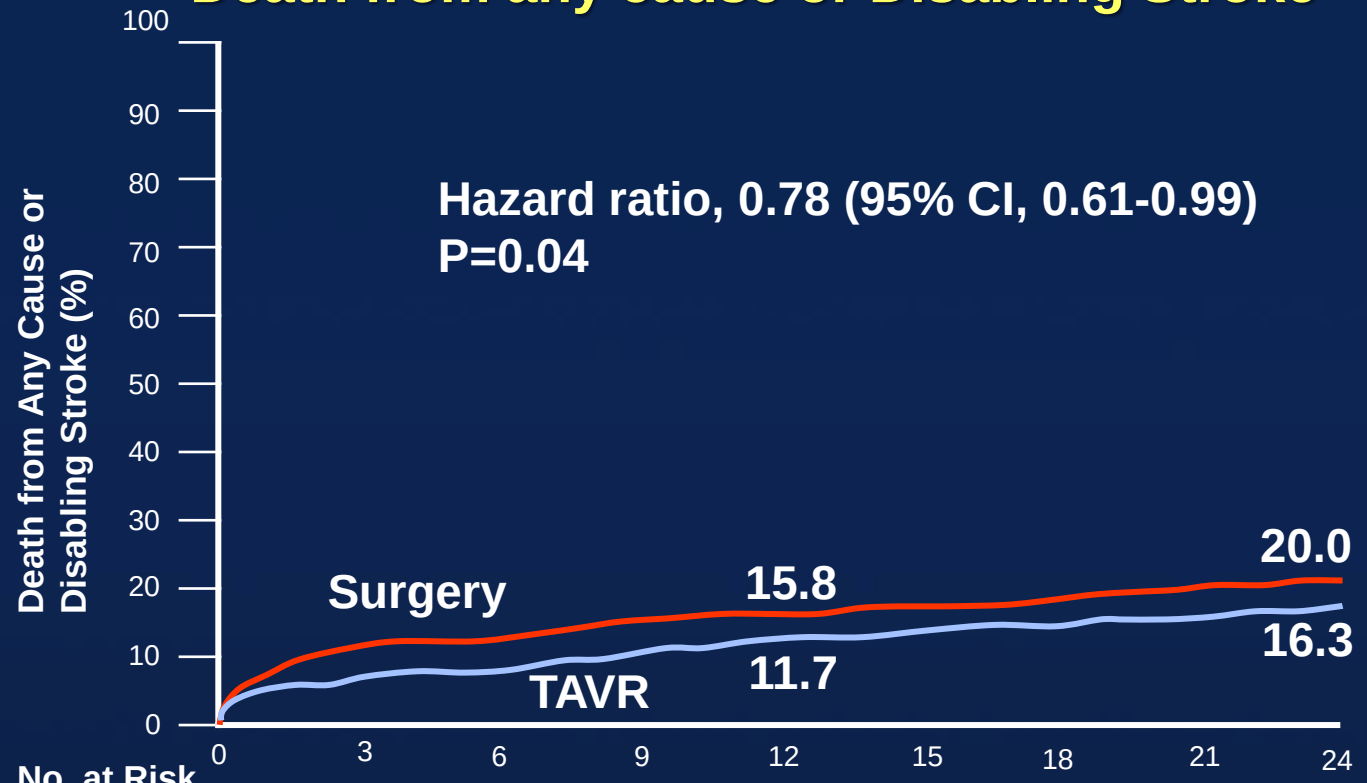
# PARTNER 2 trial : Intermediate risk




Martin B. Leon et al NEJM 2016

# PARTNER 2 trial : Intermediate risk

## Transfemoral Access Cohort
### Death from any cause or Disabling Stroke




**No. at Risk**

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| TAVR | 1011 | 918 | 901 | 870 | 842 | 825 | 811 | 801 | 774 |
| Surgery | 1021 | 838 | 812 | 783 | 770 | 747 | 735 | 717 | 695 |

Martin B. Leon et al NEJM 2016

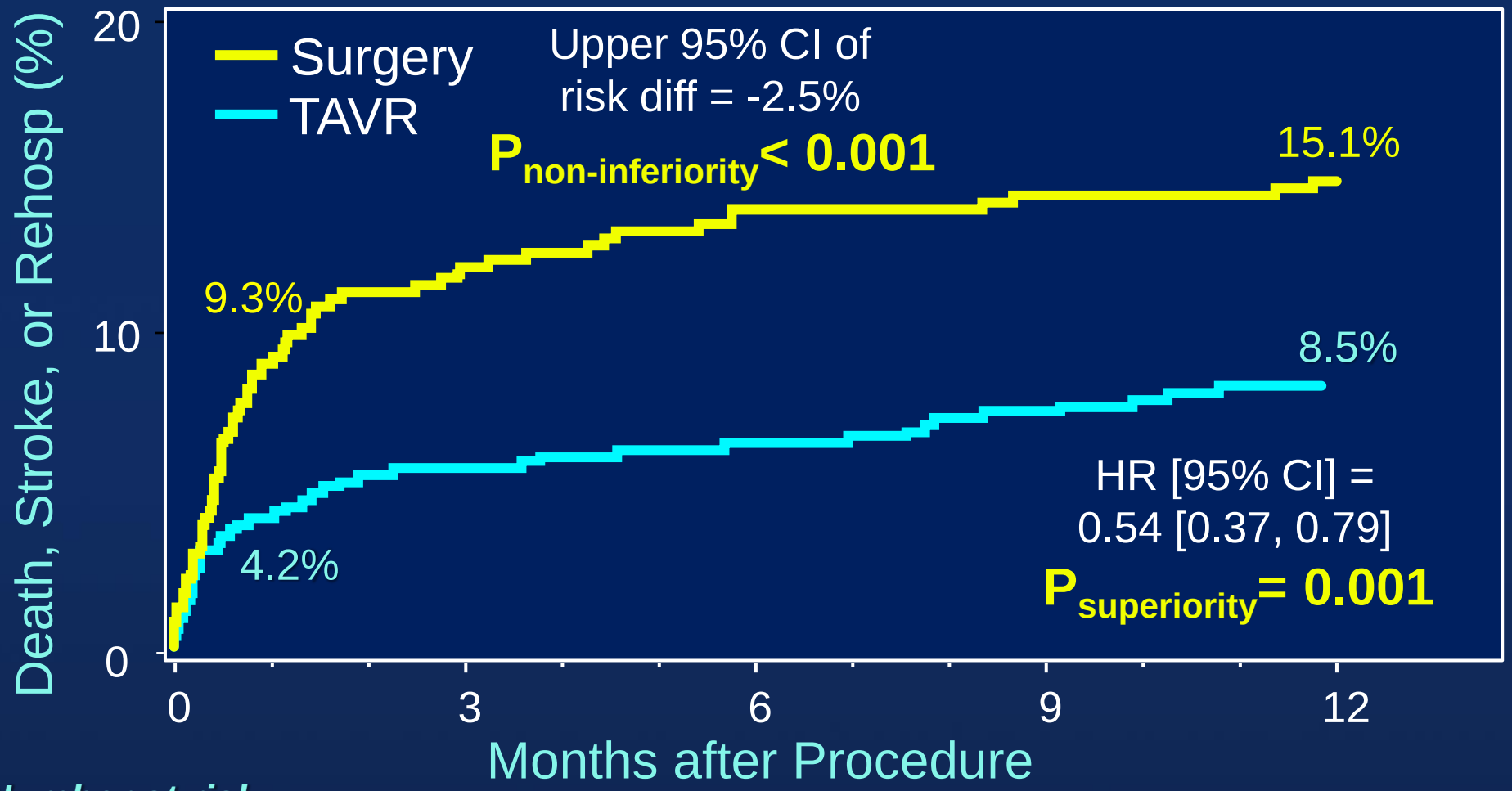
THE PARTNER 3 TRIAL

# PARTNER 3

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

# PARTNER 3 trial

## Primary Endpoint

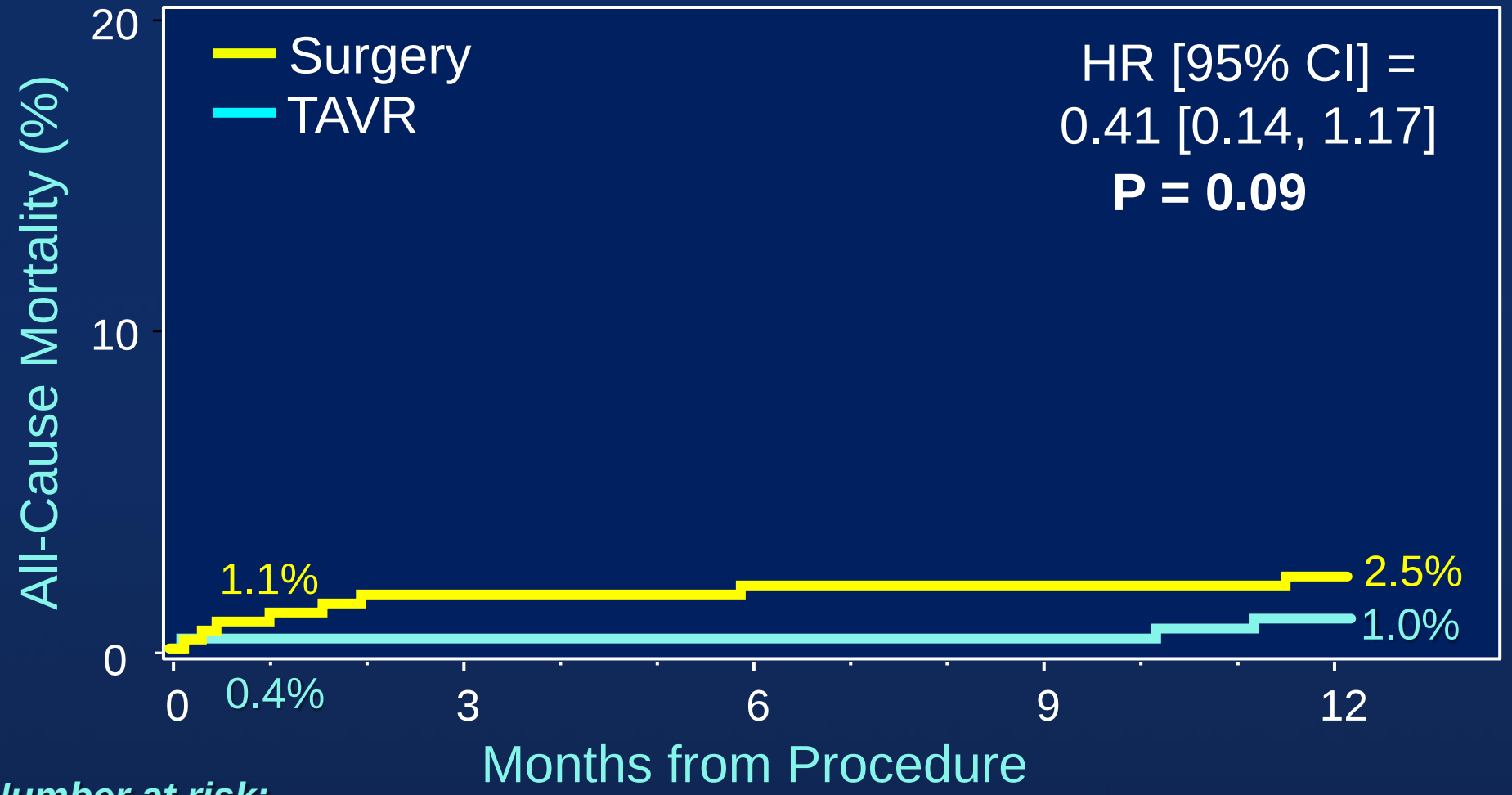



***Number at risk:***

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

# PARTNER 3 trial

## All-Cause Mortality

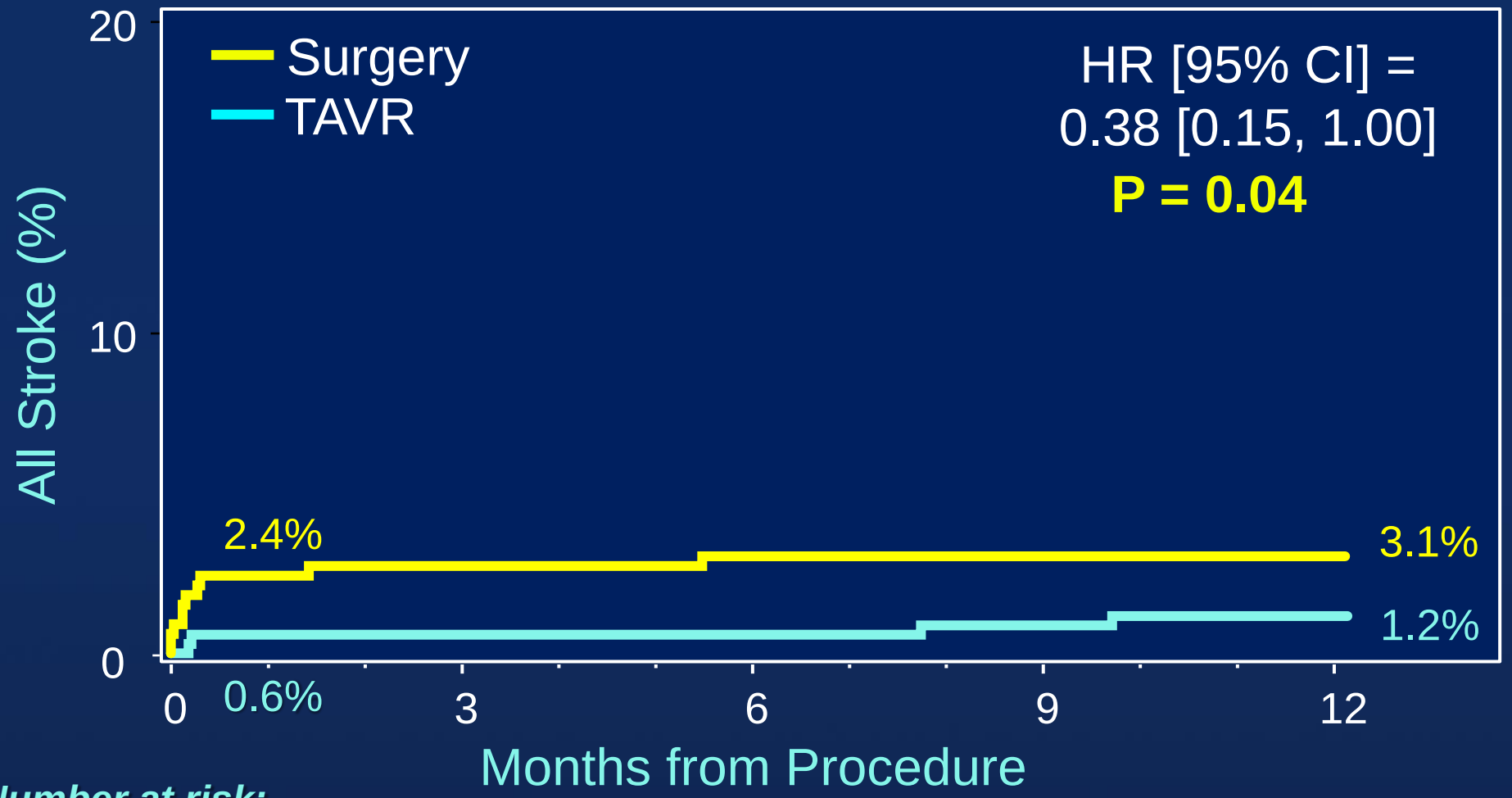



***Number at risk:***

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

# PARTNER 3 trial

## All Stroke

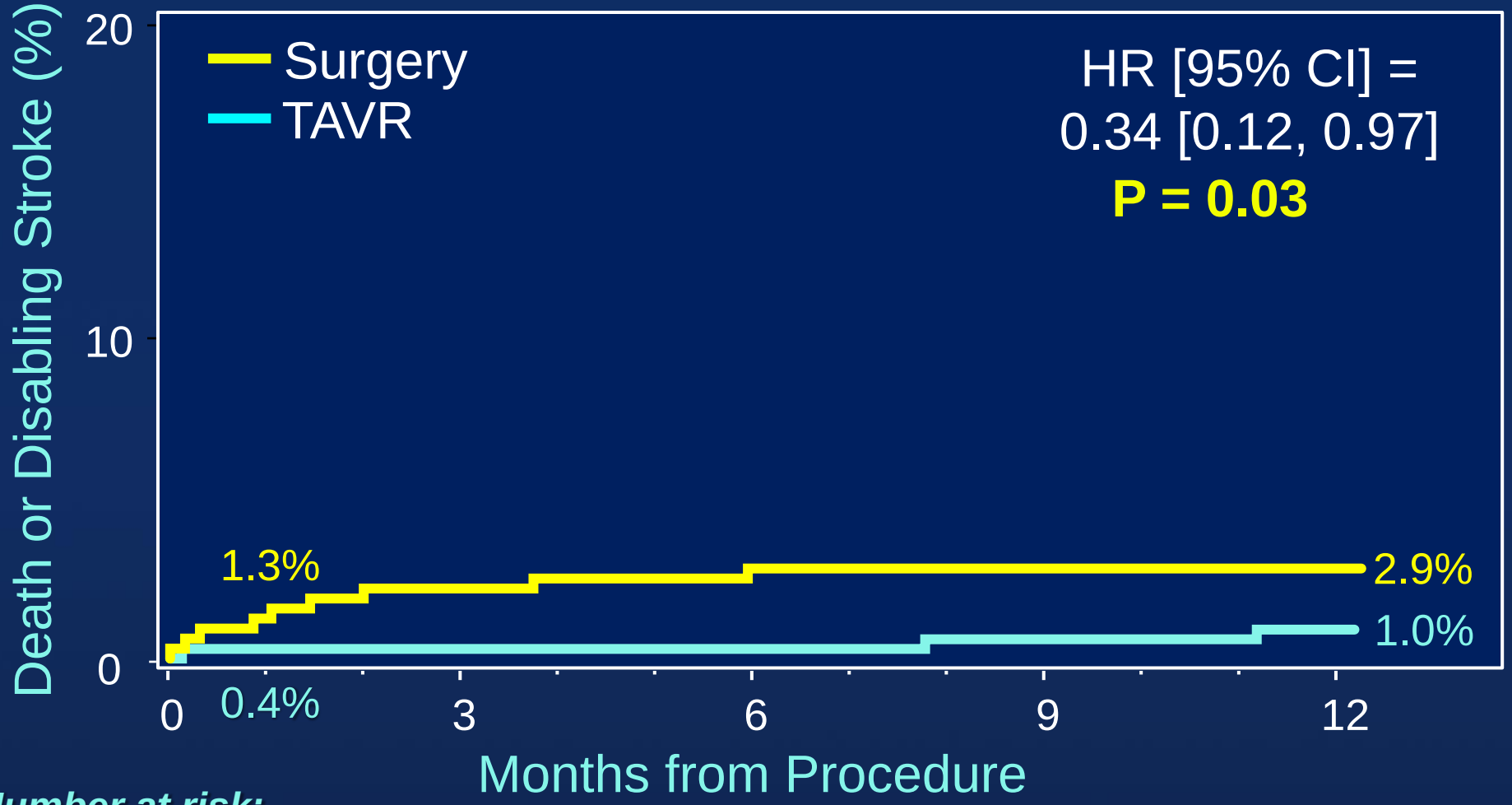



***Number at risk:***

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

# PARTNER 3 trial

## Death or Disabling Stroke

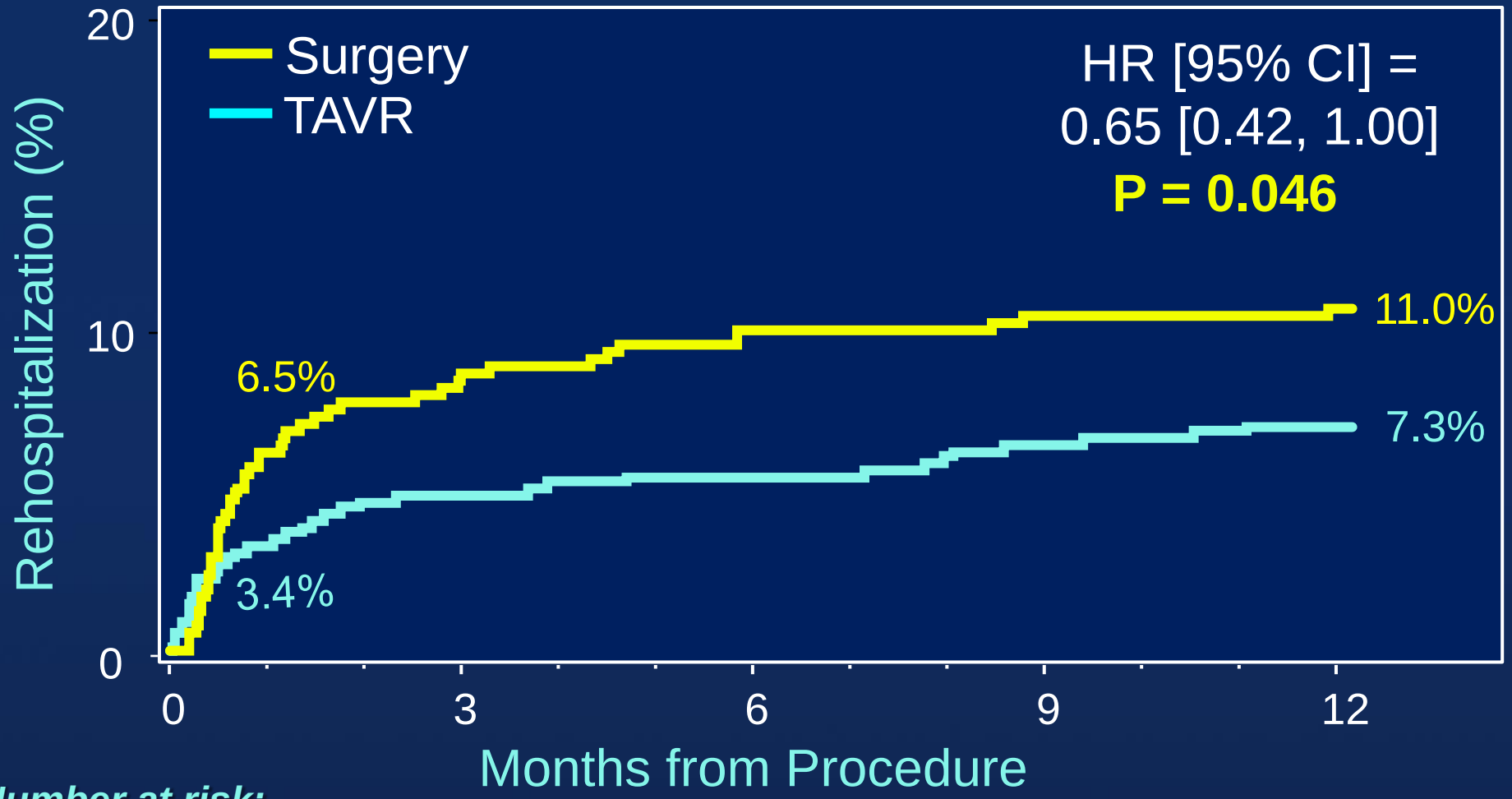



***Number at risk:***

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

# PARTNER 3 trial

## Rehospitalization



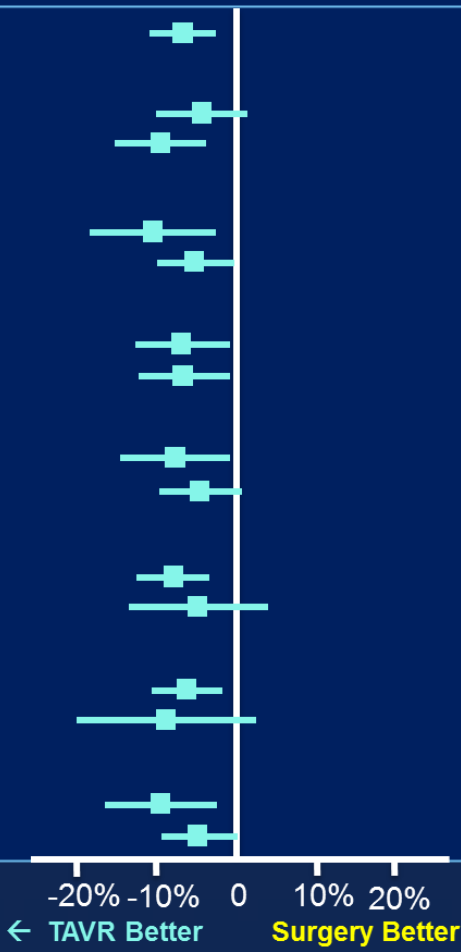

***Number at risk:***

| | | | | | | |
|---|---|---|---|---|---|---|
| **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

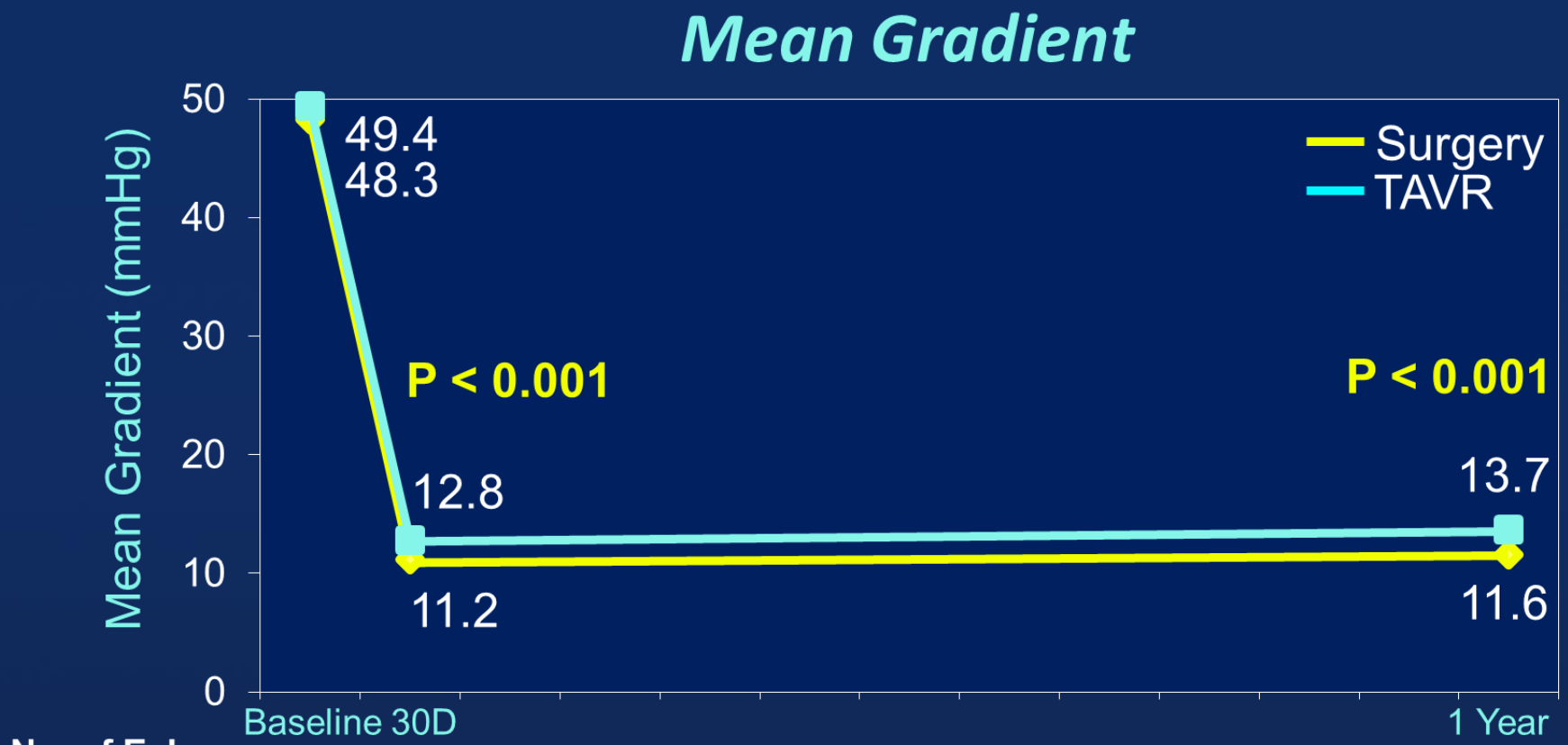
| Outcomes | 30 Days | | | 1 Year | | |
|---|---|---|---|---|---|---|
| | TAVR (N=496) | Surgery (N=454) | P-value | TAVR (N=496) | Surgery (N=454) | P-value |
| Bleeding - Life-threat/Major | 3.6% (18) | 24.5% (111) | <0.001 | 7.7% (38) | 25.9% (117) | <0.001 |
| Major Vascular Complics | 2.2% (11) | 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

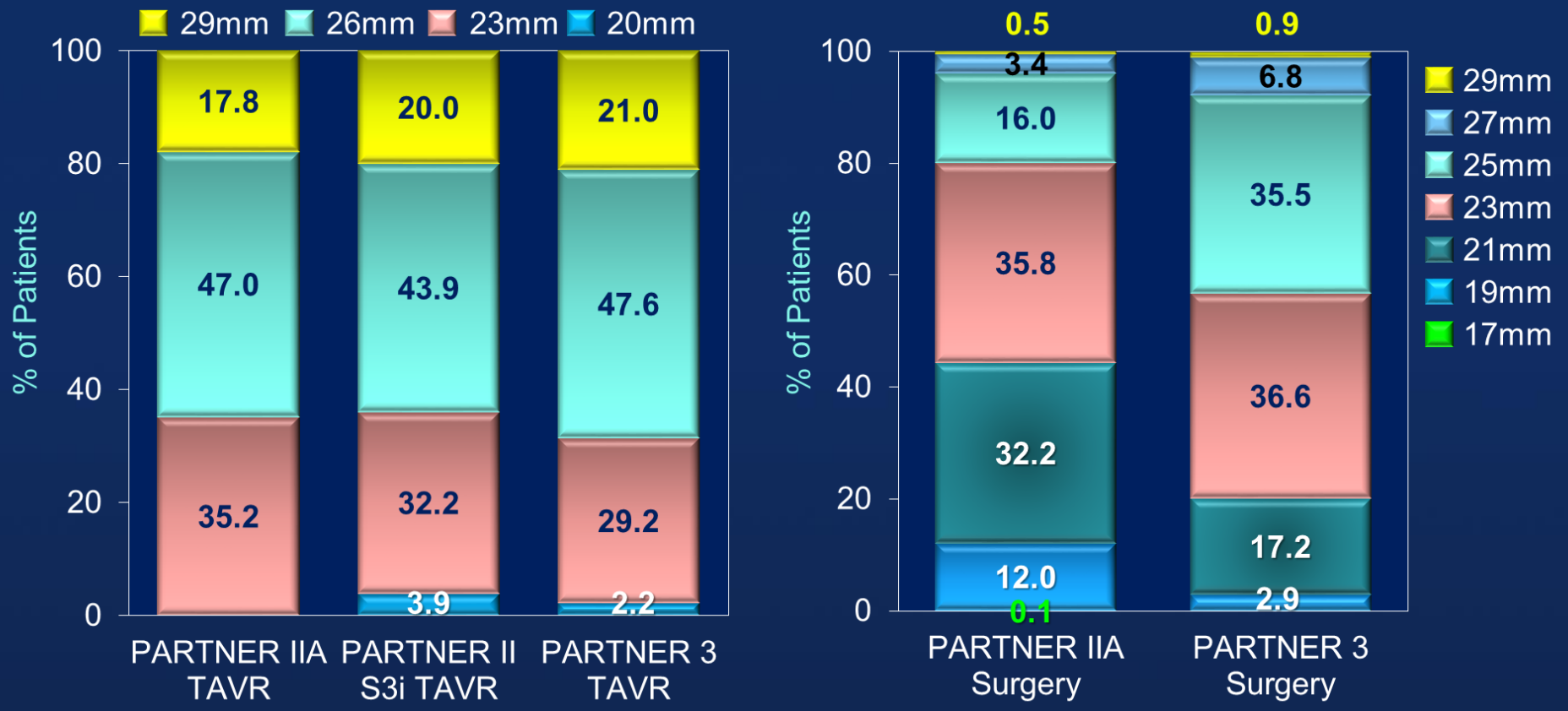
## Echocardiography Findings


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

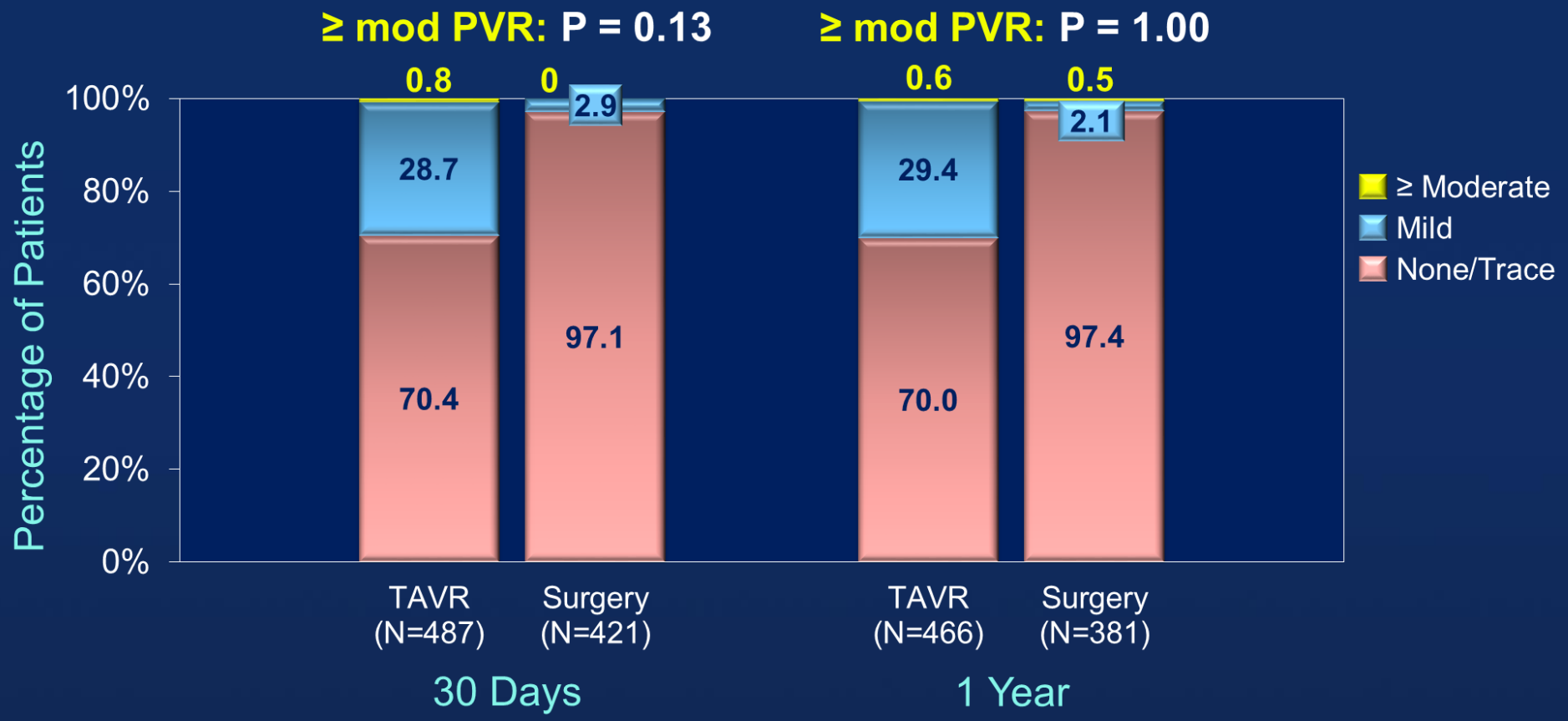
P-values are based on the ANCOVA for TAVR vs Surgery adjusted by baseline.

# The PARTNER trials

## *Valve Size Distribution*



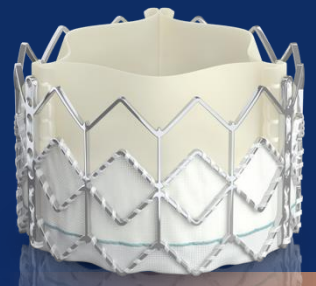
# PARTNER 3 trial
## Paravalvular Regurgitation




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

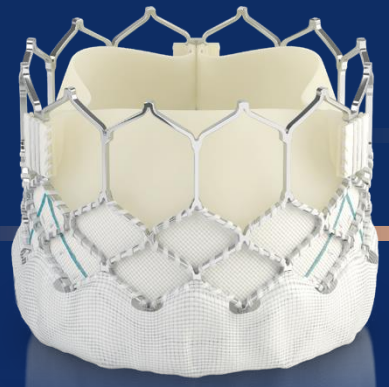
# SAPIEN 3 Ultra

# Changes in Sapien Series

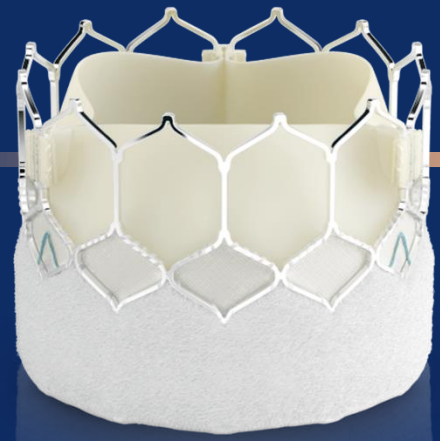


Save lives, starting with the sickest patients

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

Ask

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

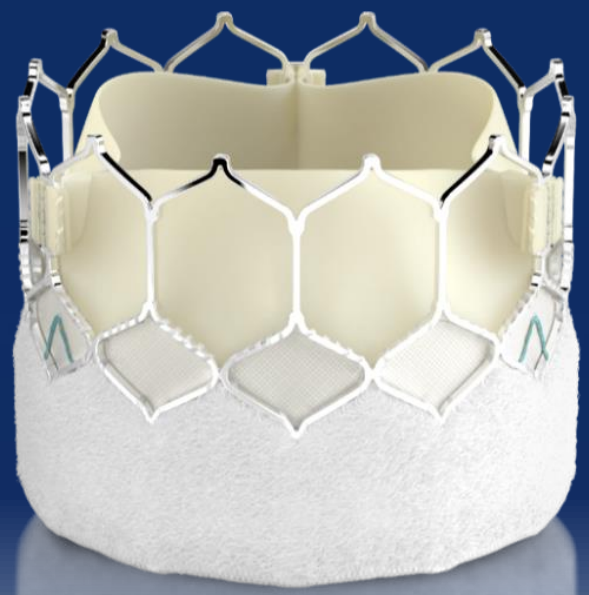
## SAPEIN 3 Ultra

| | 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*

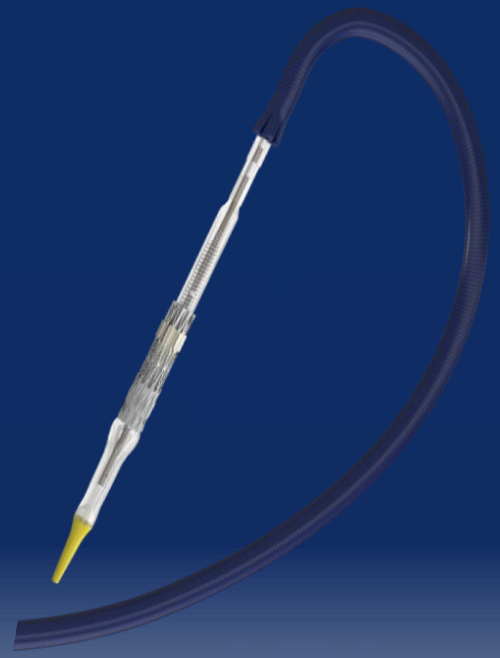
CT, computed tomography; TEE, Transesophageal echocardiogram

# Edwards SAPIEN 3 Ultra System



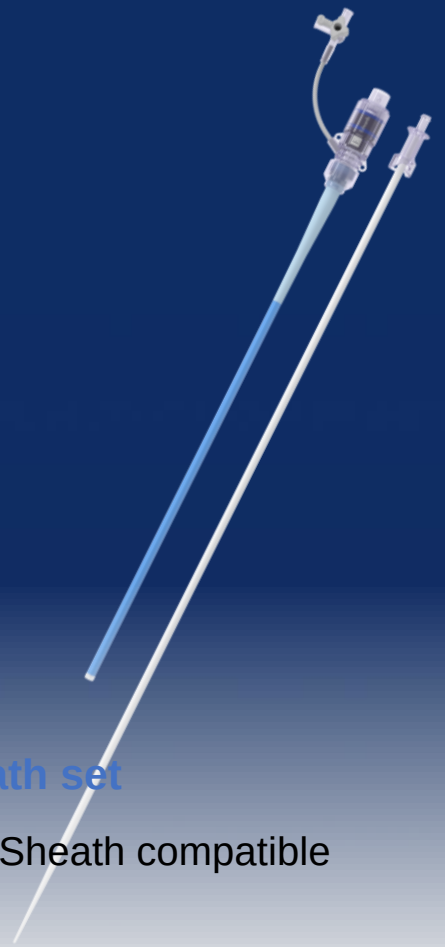
**SAPIEN 3 Ultra valve[1]**

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



**Commander delivery system**

Physician controlled dual articulation with tapered distal tip



**eSheath set**

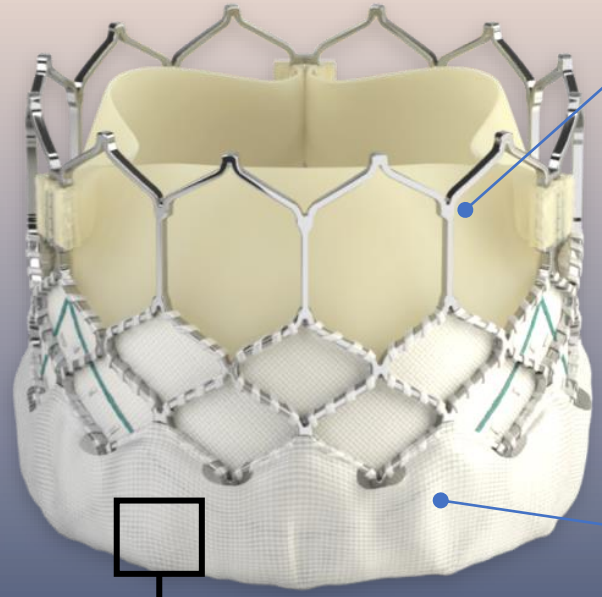
14Fr eSheath compatible

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

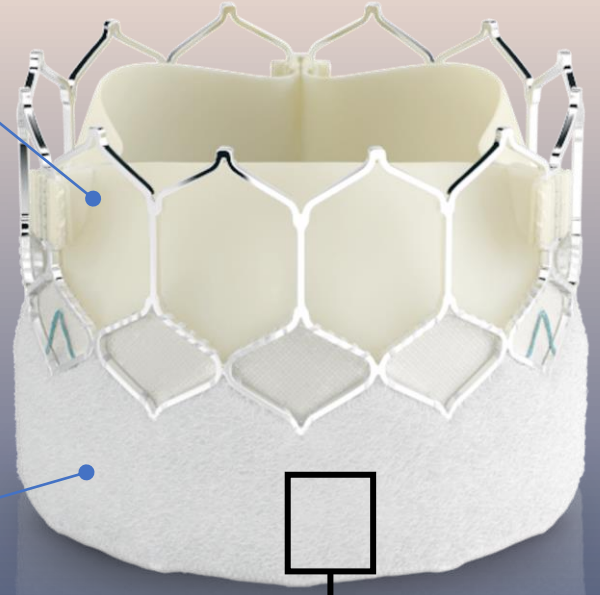
# SAPIEN 3 Ultra valve vs SAPIEN 3

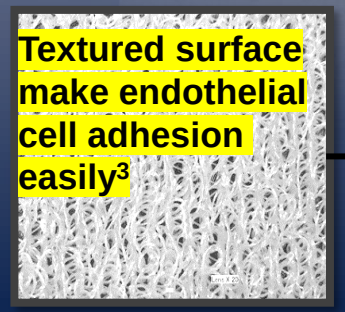
Building on the standard in TAVI to meet the needs of today

## 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)

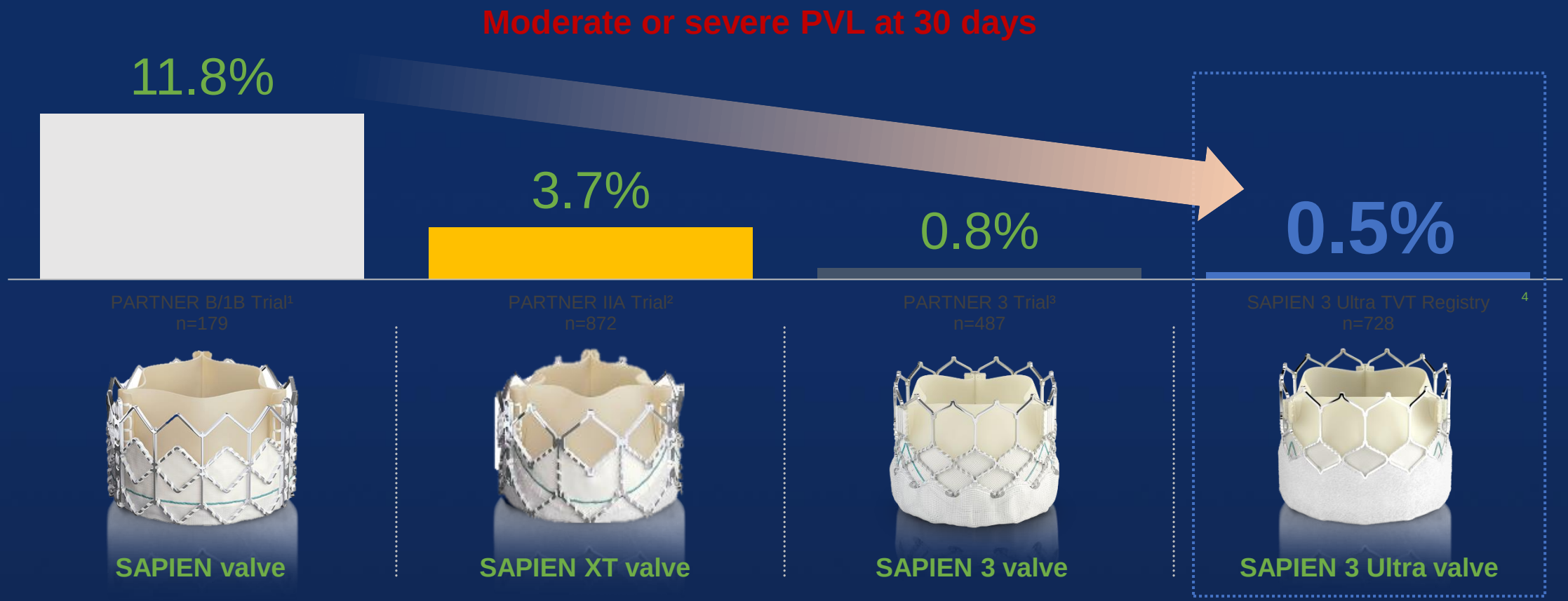
  : Enhance healing and endothelialization[3,4]



CVRF

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

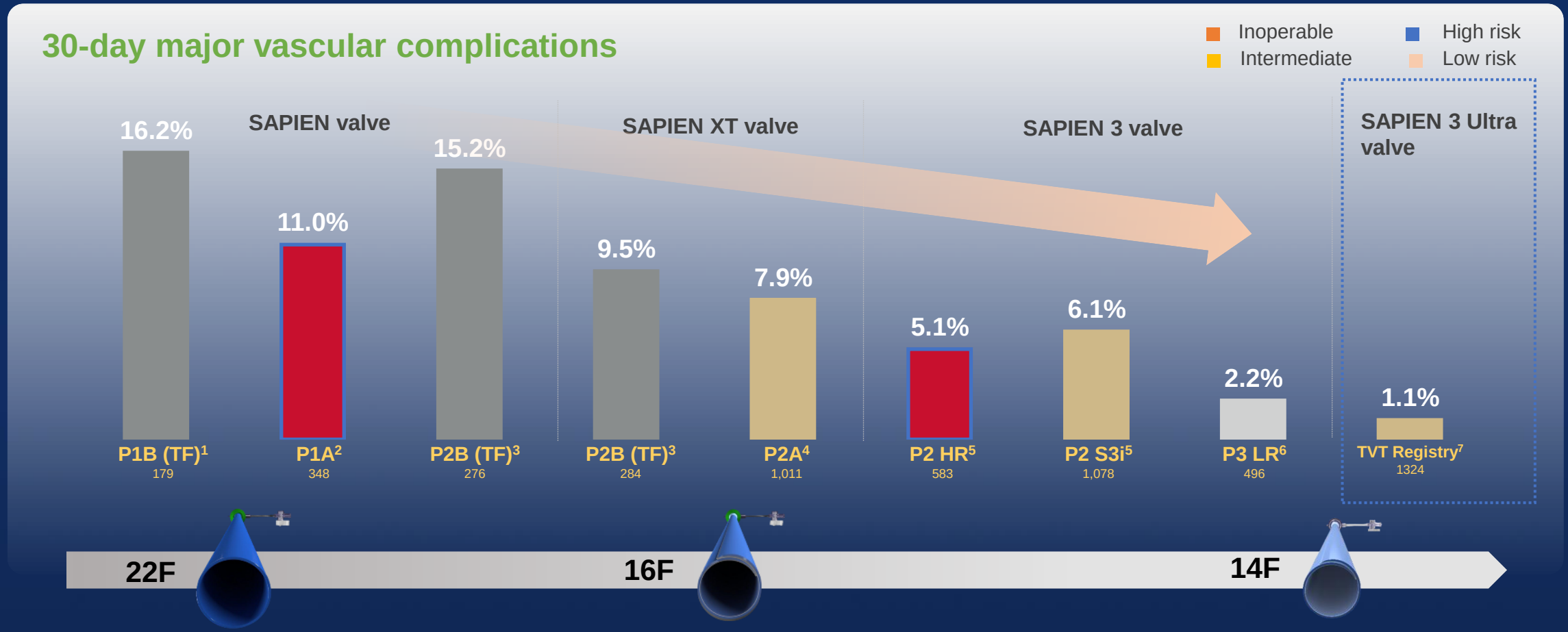
# Decreased Significant PVL





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

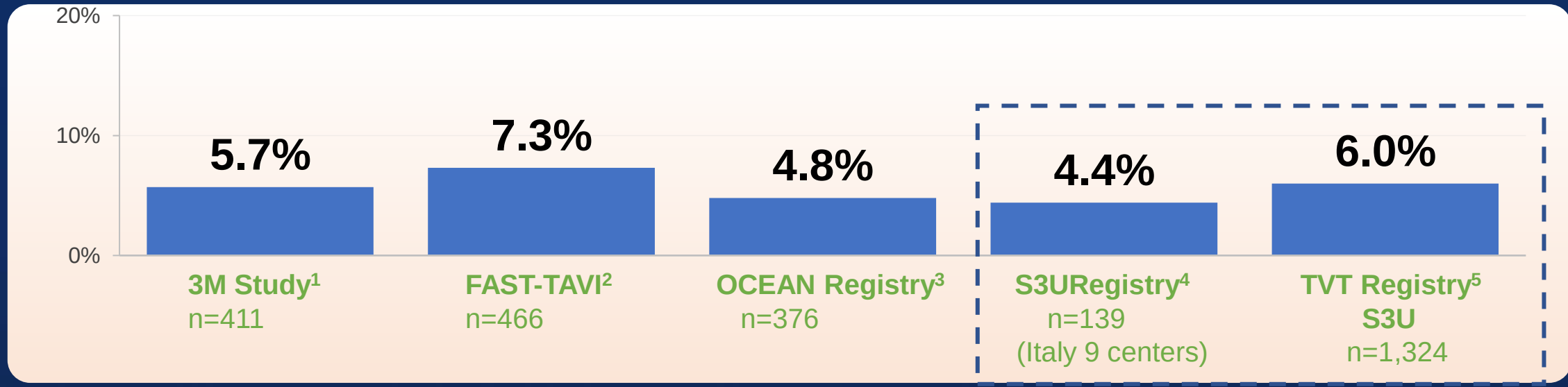




1. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med*. 2010;363(17):1597-1607.
2. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus Surgical Aortic-Valve Replacement in High-Risk Patients. *N Engl 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)

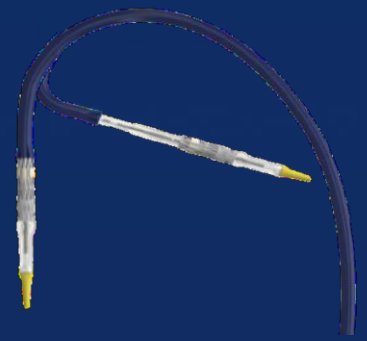
| n=1,324 | S3U TAVI[1] |
|---|---|
| All-cause mortality | 0.9% |
| All-cause stroke | 1.2% |
| Rehospitalization | 4.4% |
| New permanent pacemaker | 6.0% |
| Major vascular complication | 1.1% |
| Life-threatening bleeding | 0.0% |



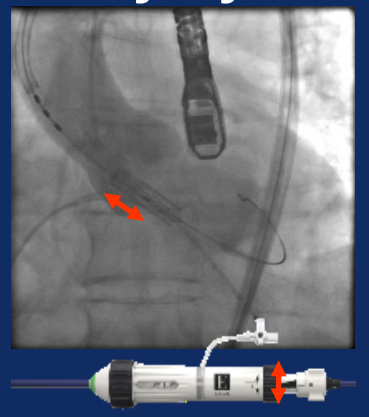
1. Nazif T, Daniels D, McCabe J, Chehab B, et al. Real-world experience with the SAPIEN 3 Ultra TAVI: A propensity matched analysis from the United States. Presented virtually at TVT Connect 2020

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

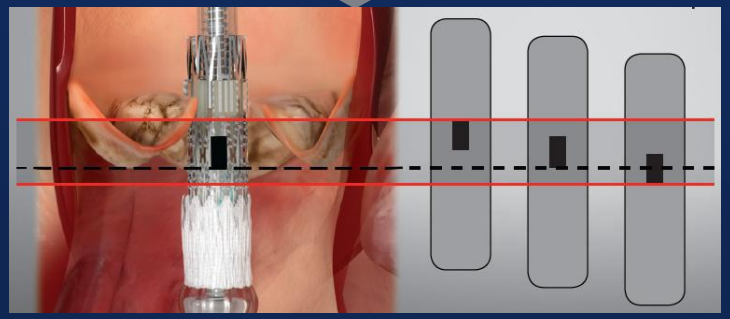
## Edwards Commander Delivery System



Dual Articulation

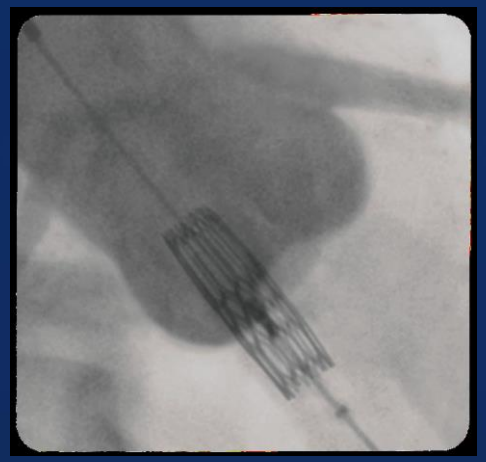
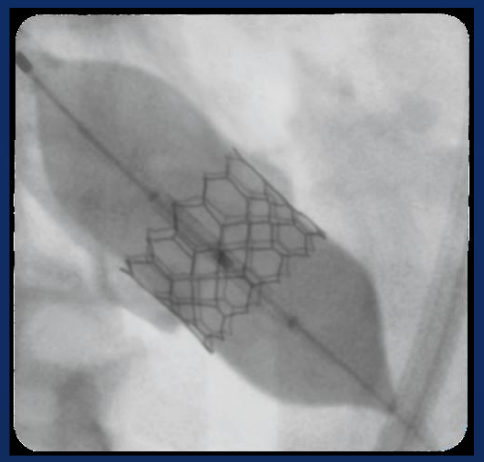
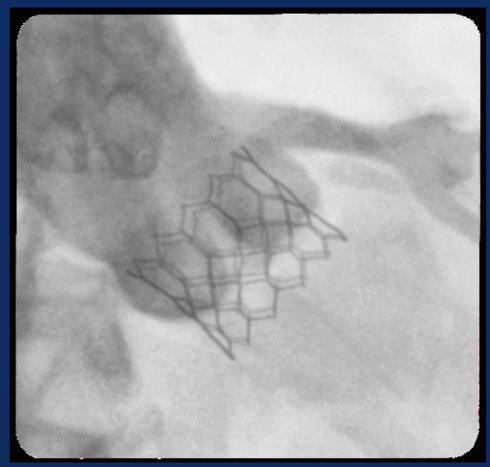


Fine Positioning



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

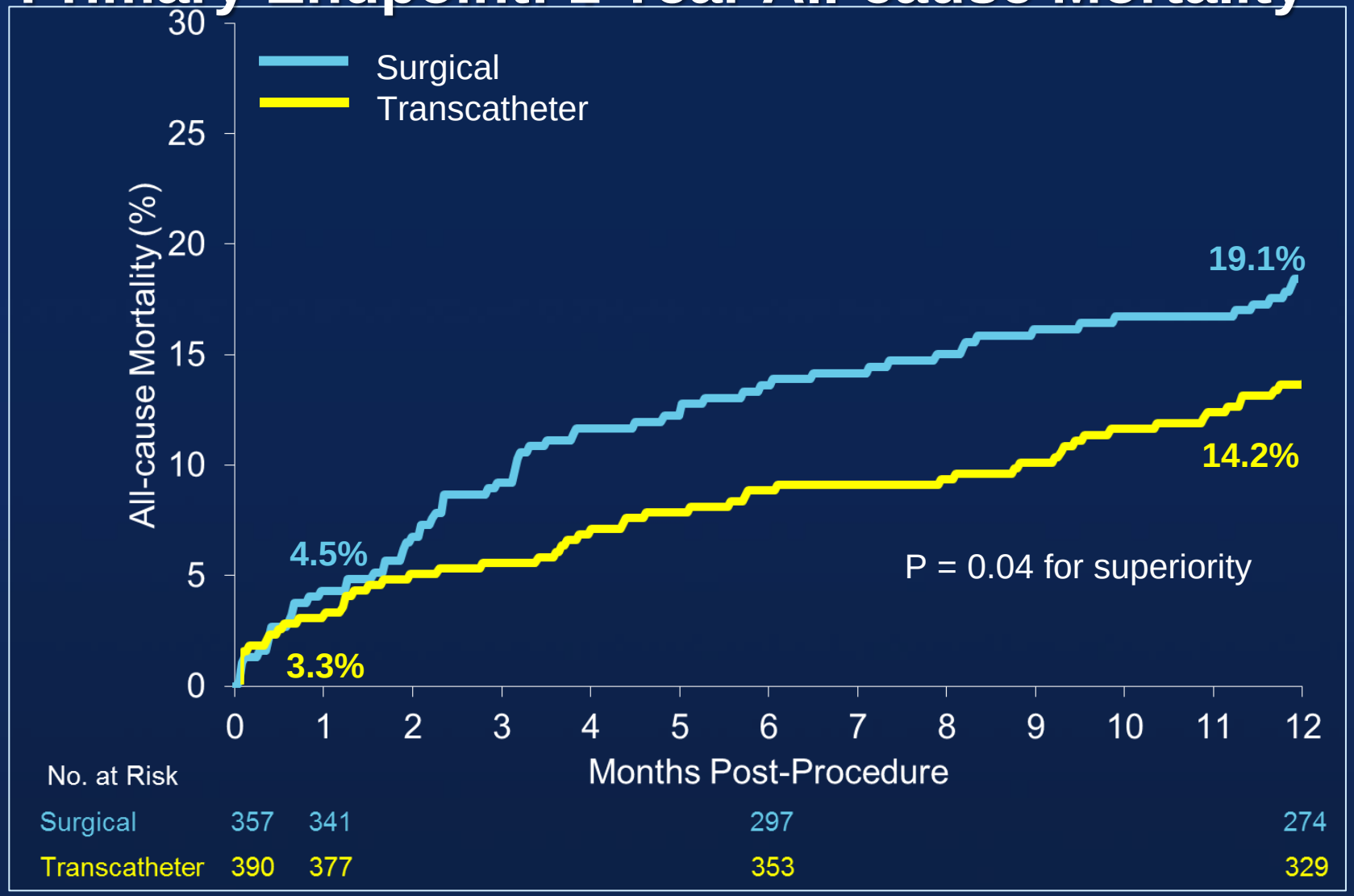
Annulus Rupture

PPM

# CoreValve Trials

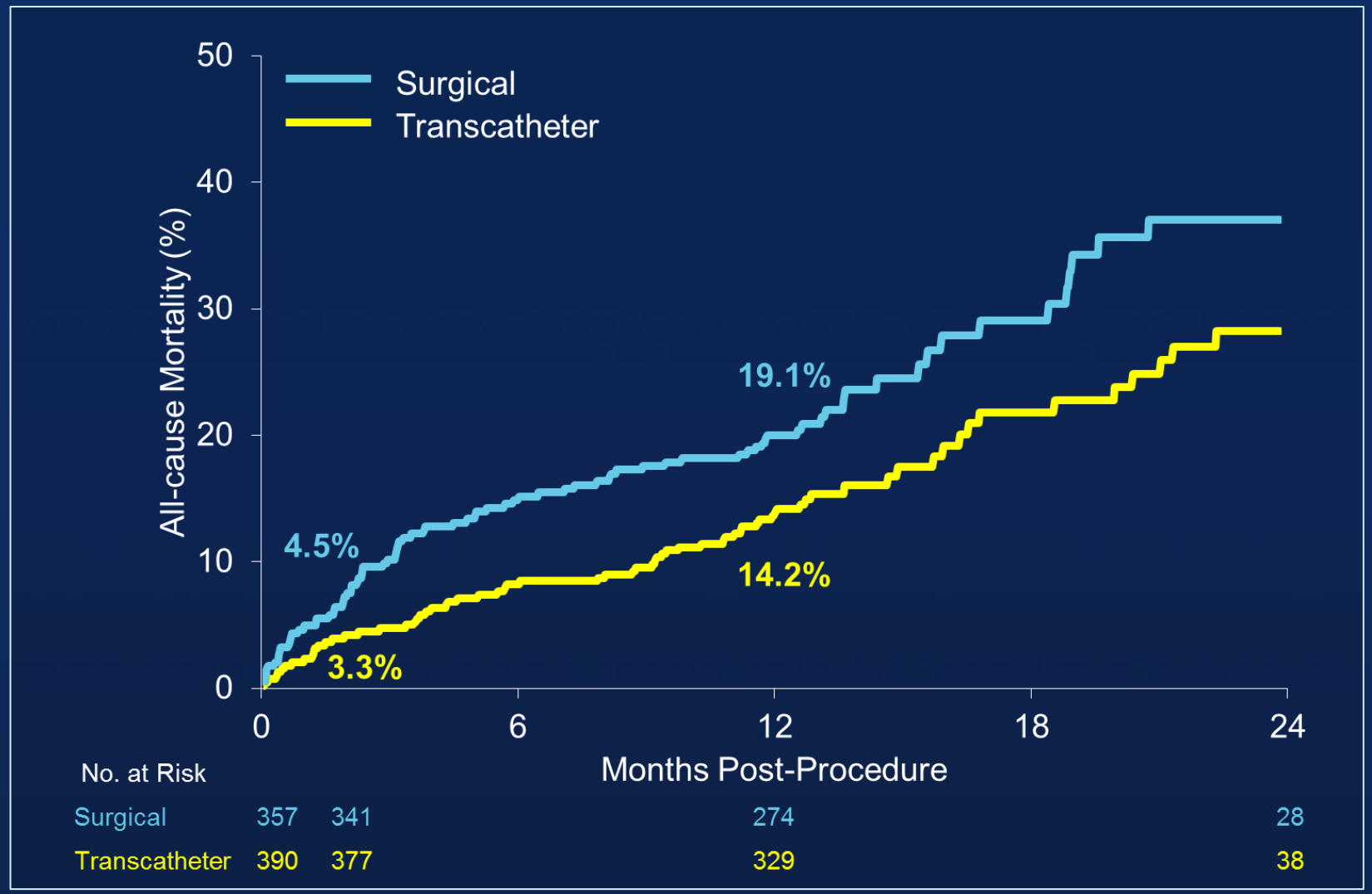
# CoreValve US Pivotal Trial

## Primary Endpoint: 1 Year All-cause Mortality



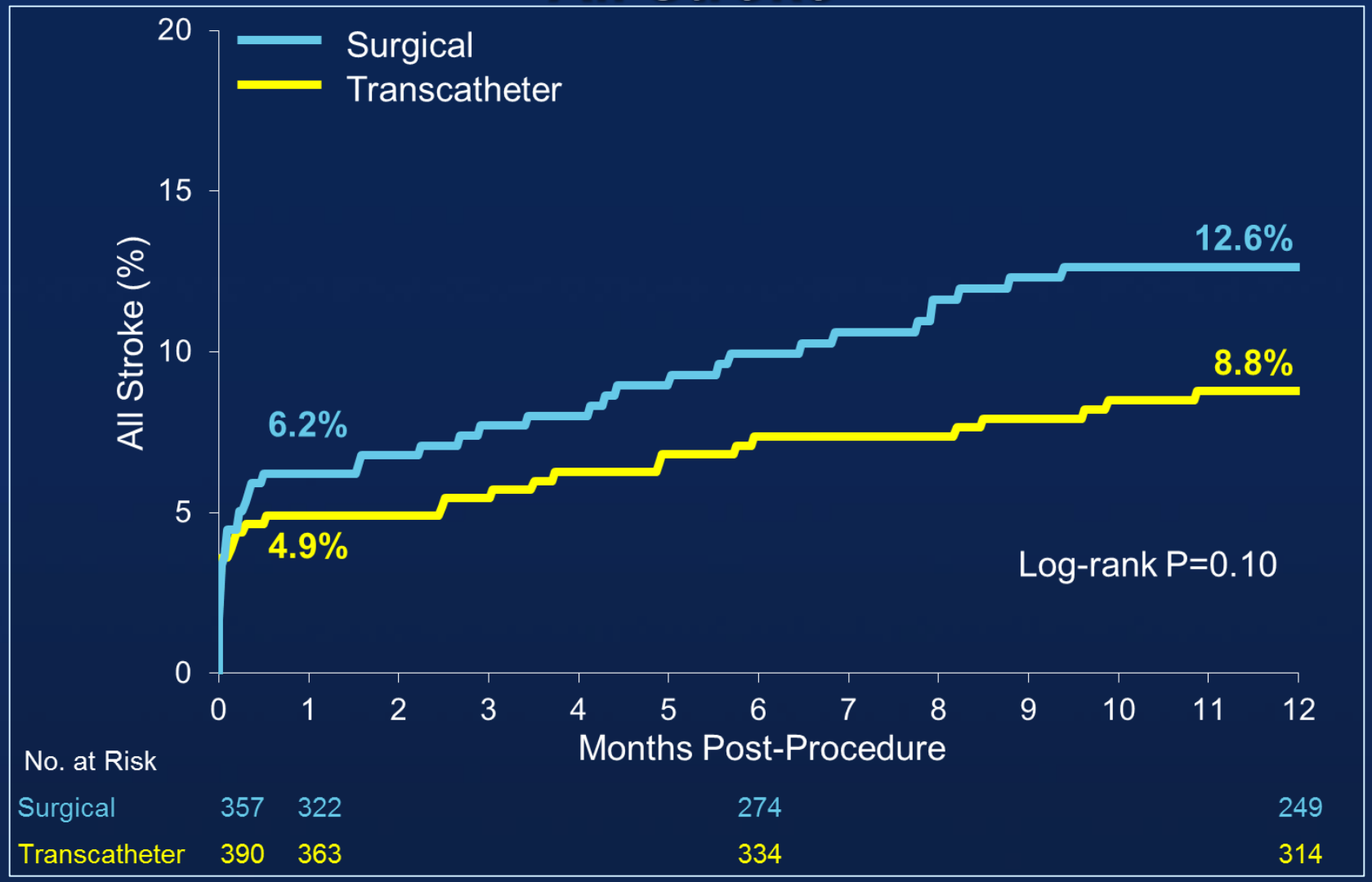
# CoreValve US Pivotal Trial

## 2-Year All-cause Mortality



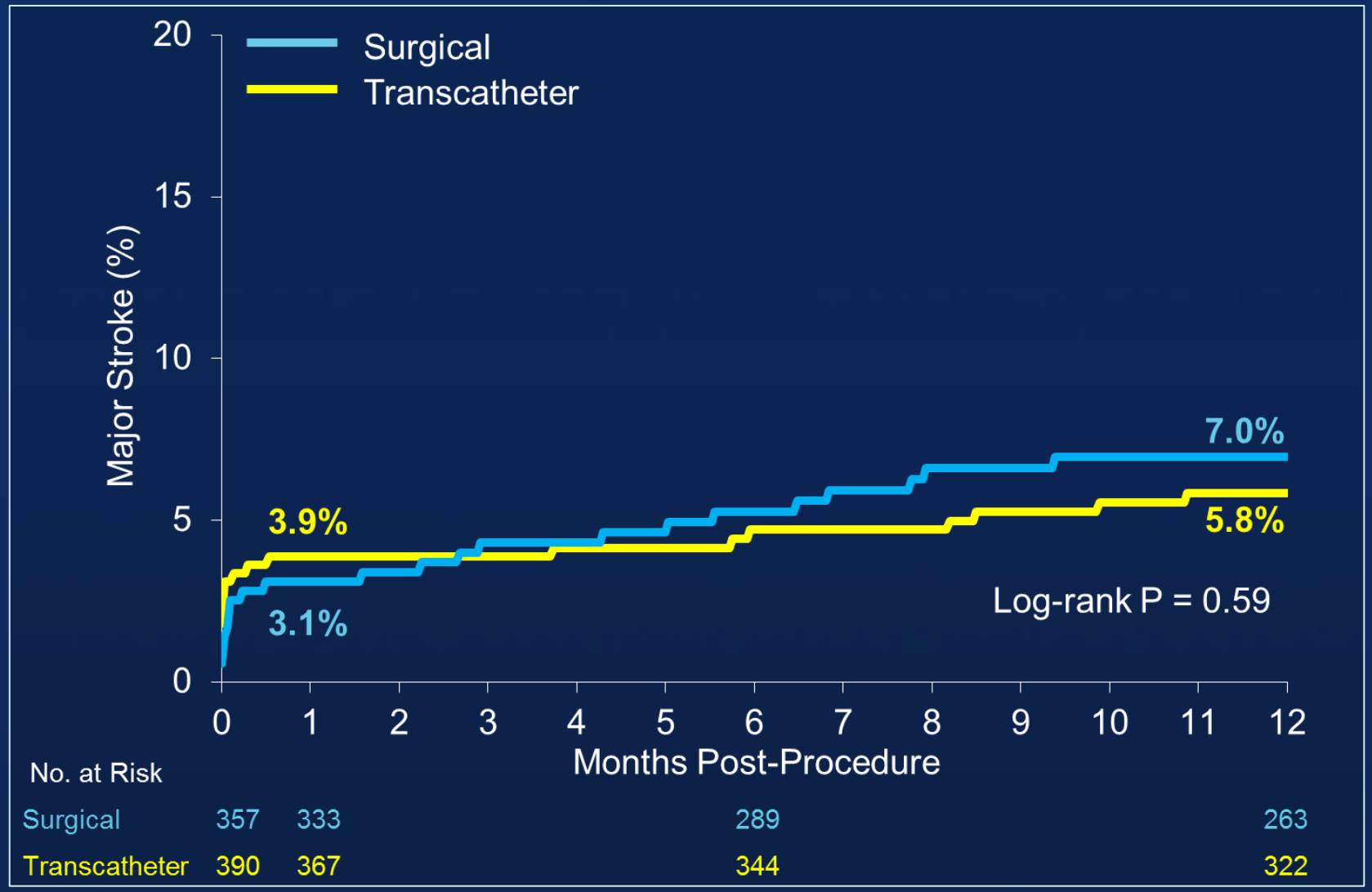
# CoreValve US Pivotal Trial

## All Stroke



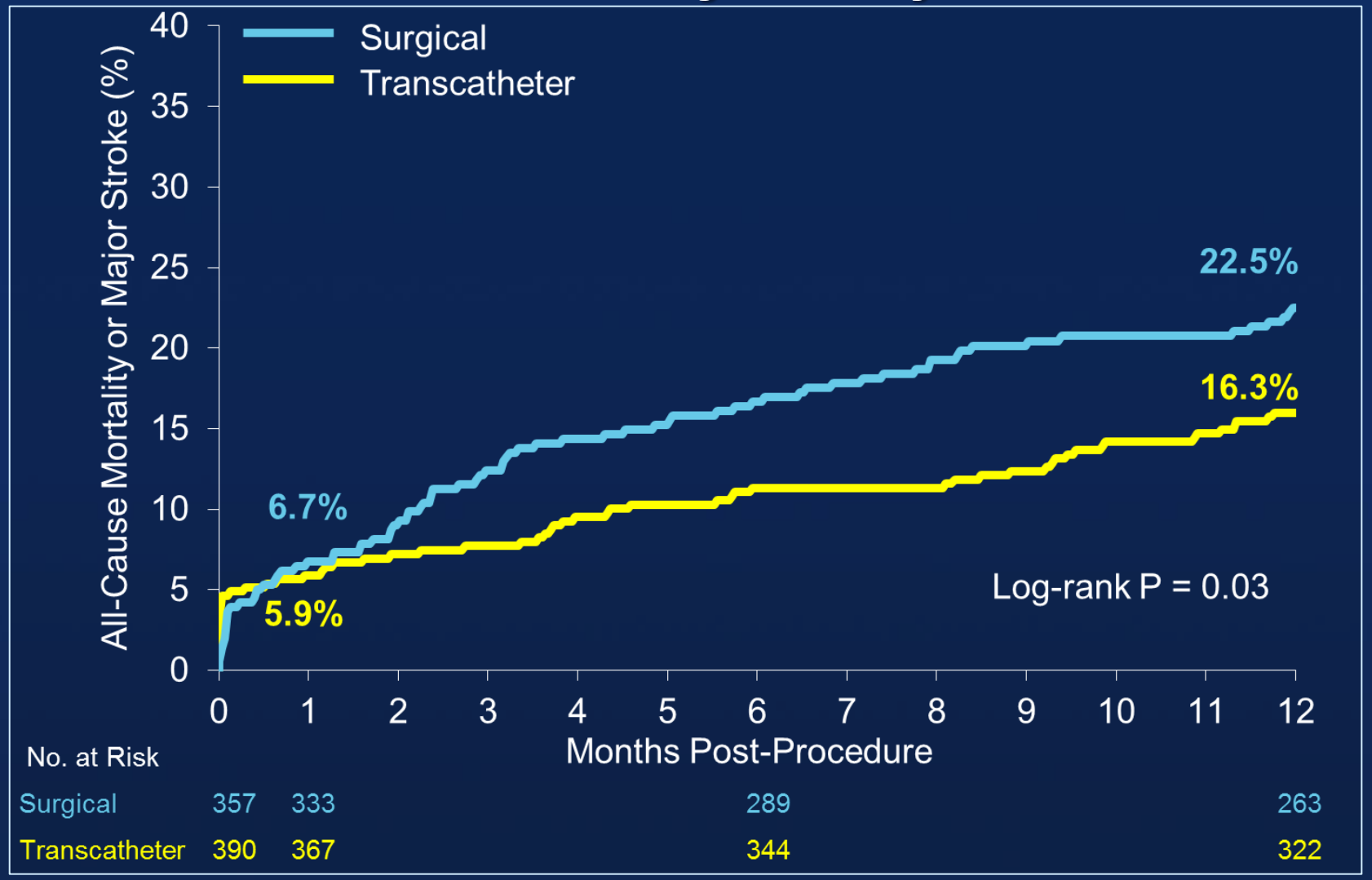
# CoreValve US Pivotal Trial

## Major Stroke



# CoreValve US Pivotal Trial

## All-Cause Mortality or Major Stroke



# CoreValve US Pivotal Trial

## Other Endpoints

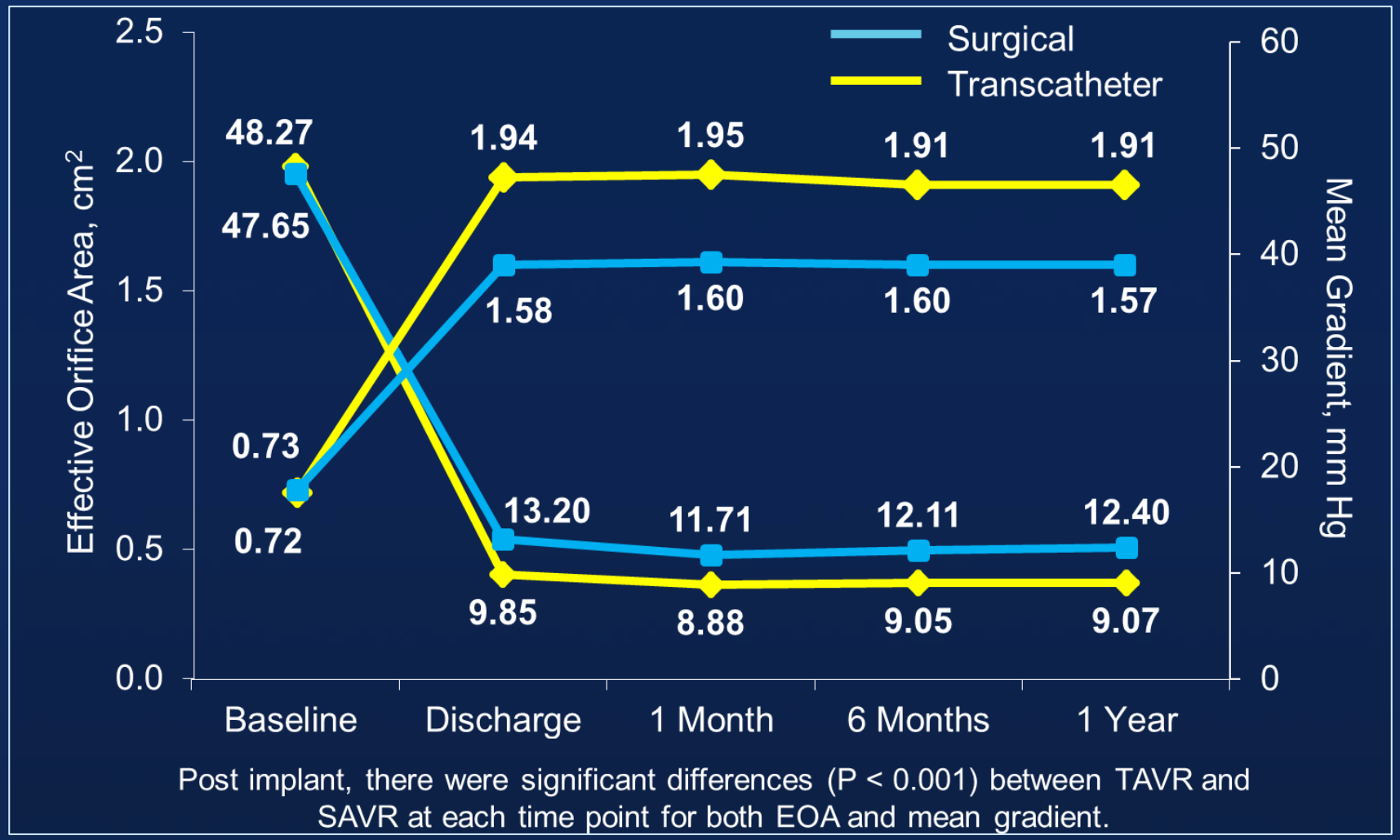
| Events* | 1 Month | | | 1 Year | | |
|---|---|---|---|---|---|---|
| | TAVR | SAVR | P Value | TAVR | SAVR | P Value |
| Vascular complications (major), % | 5.9 | 1.7 | 0.003 | 6.2 | 2.0 | 0.004 |
| Pacemaker implant, % | 19.8 | 7.1 | <0.001 | 22.3 | 11.3 | <0.001 |
| Bleeding (life threatening or 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

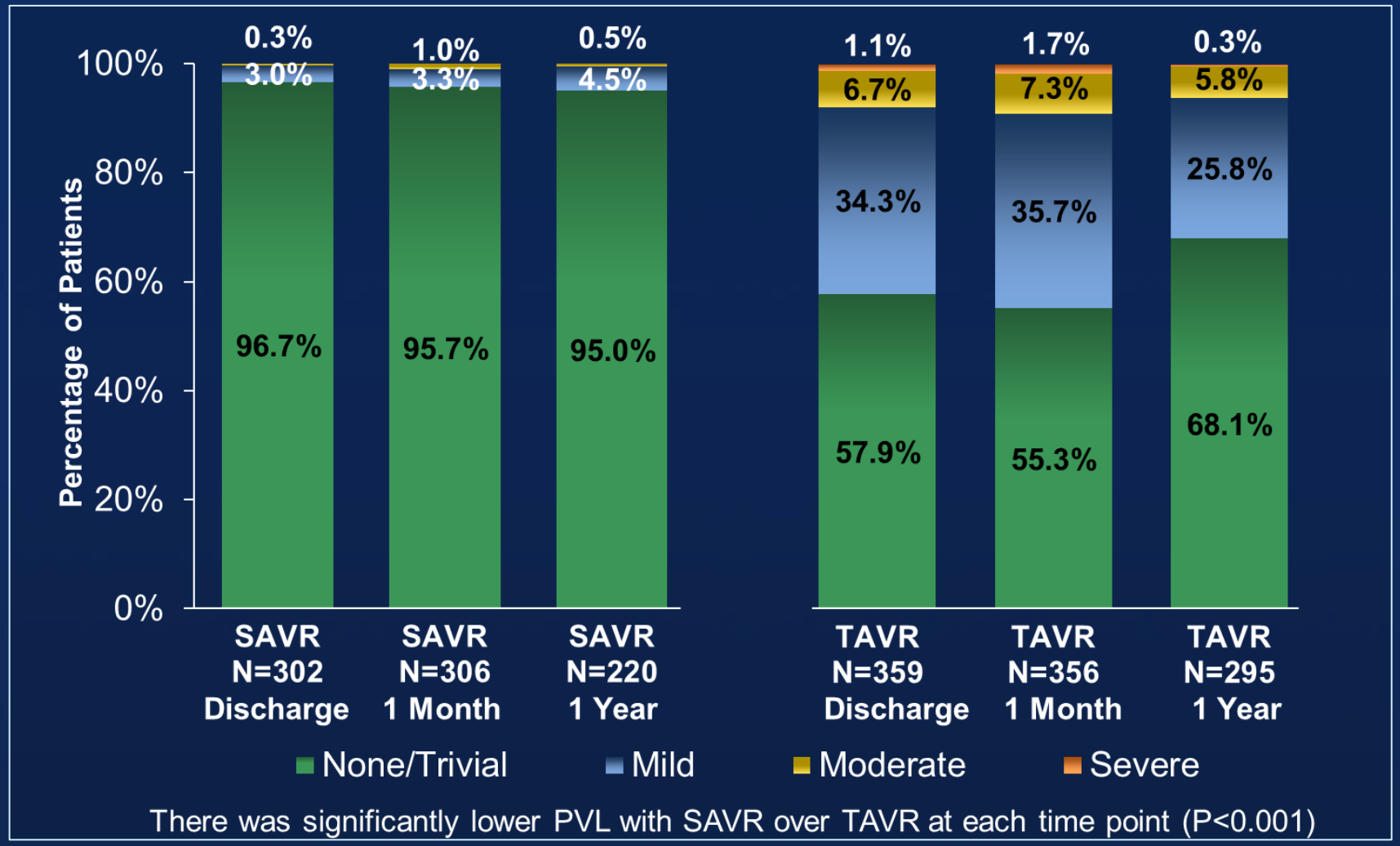
## Echocardiographic Findings




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

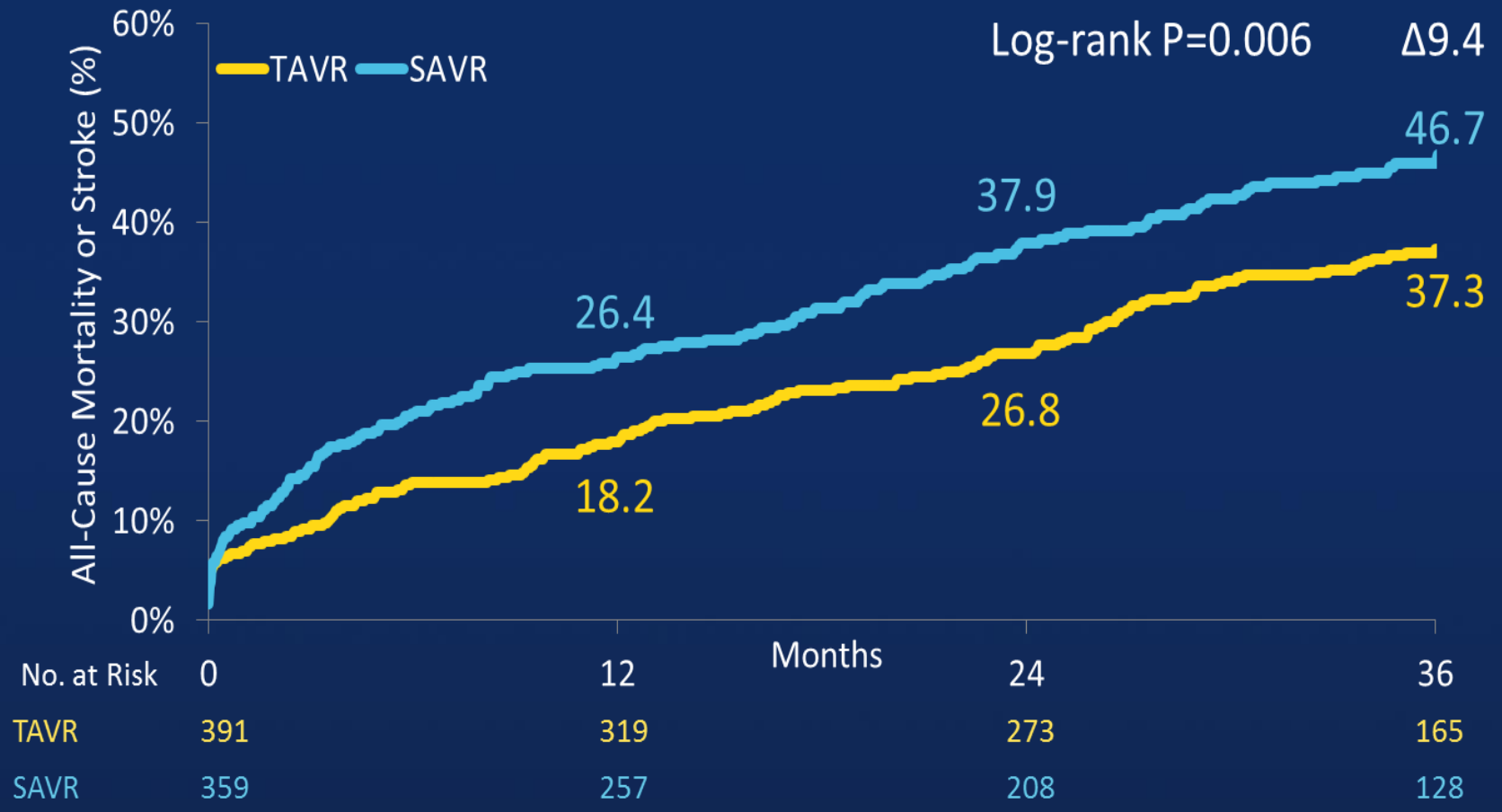
## Paravalvular Regurgitation




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

# CoreValve US Pivotal Trial– 3 year result

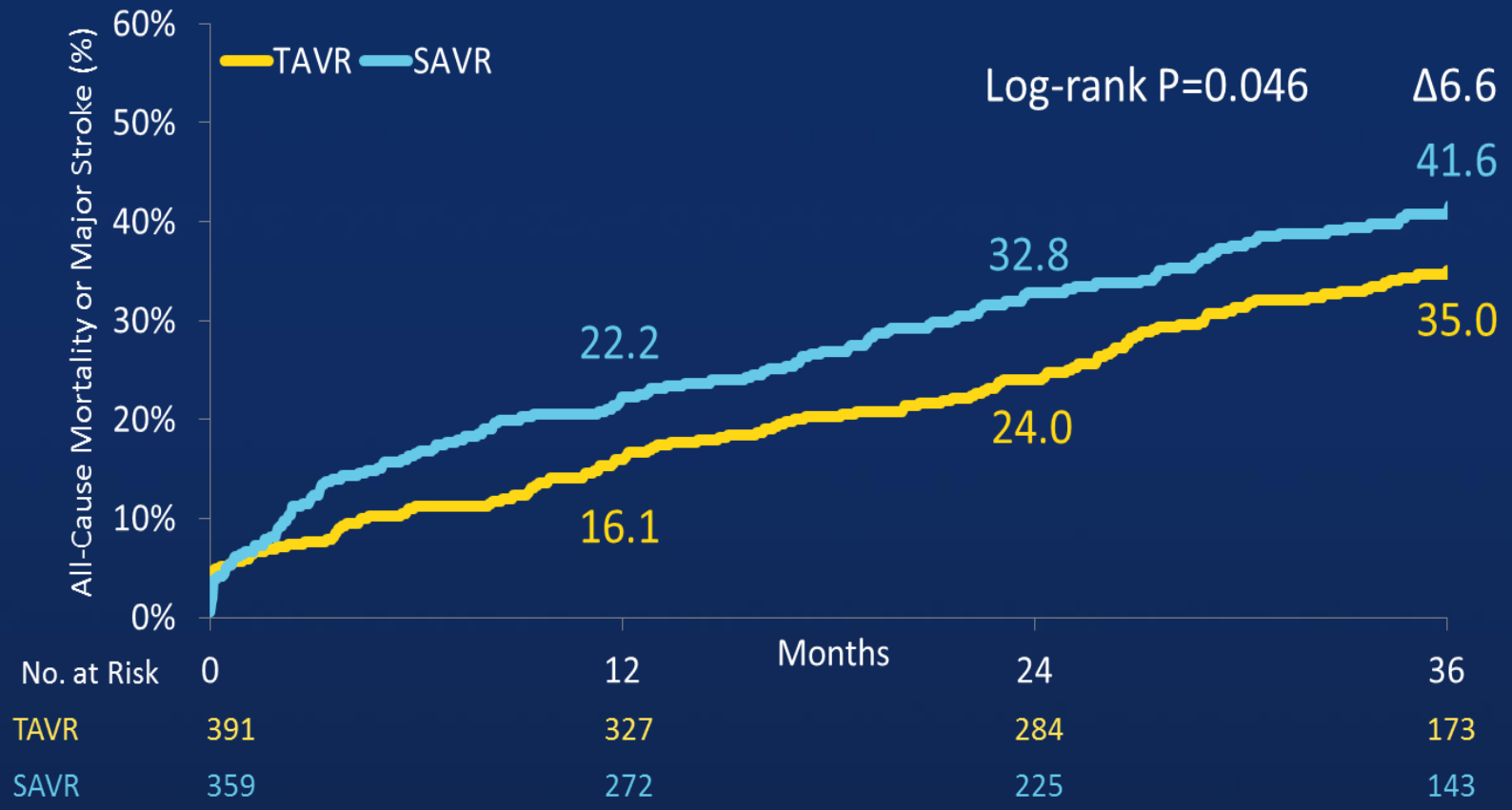
## All-Cause Mortality or Stroke




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

# CoreValve US Pivotal Trial– 3 year result

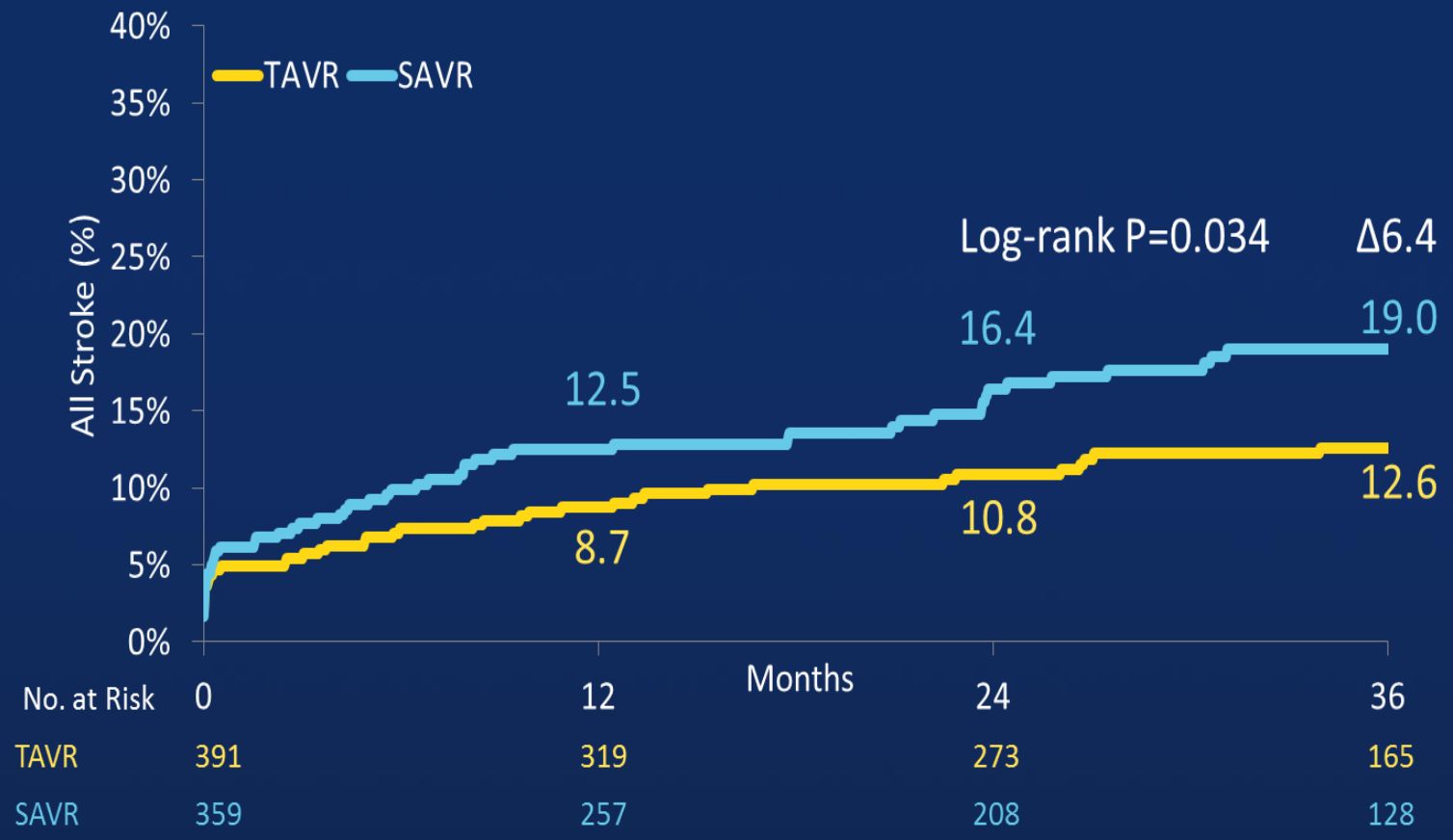
## All-Cause Mortality or Major Stroke




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

# CoreValve US Pivotal Trial– 3 year result

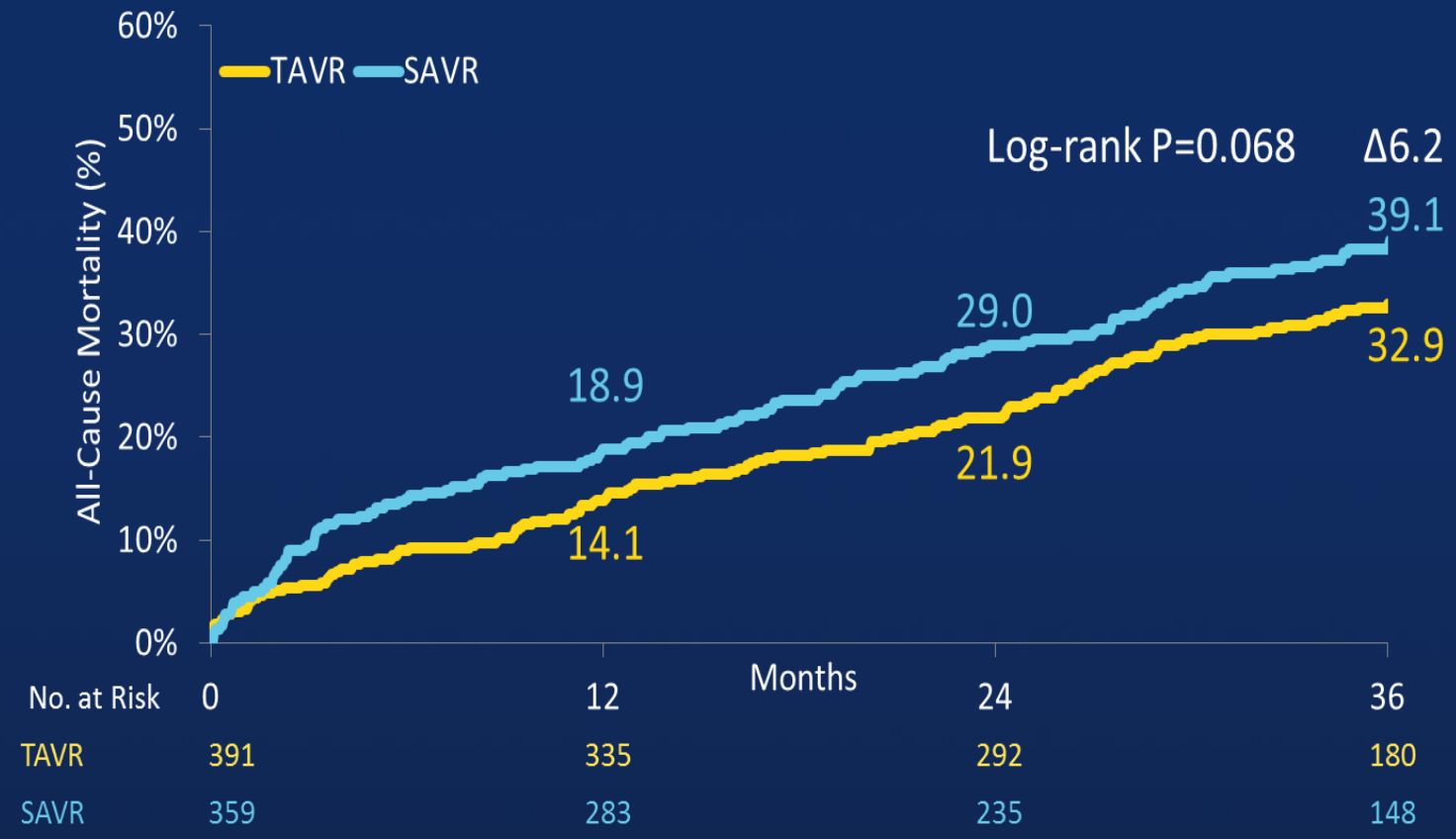
## All Stroke




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

# CoreValve US Pivotal Trial– 3 year result

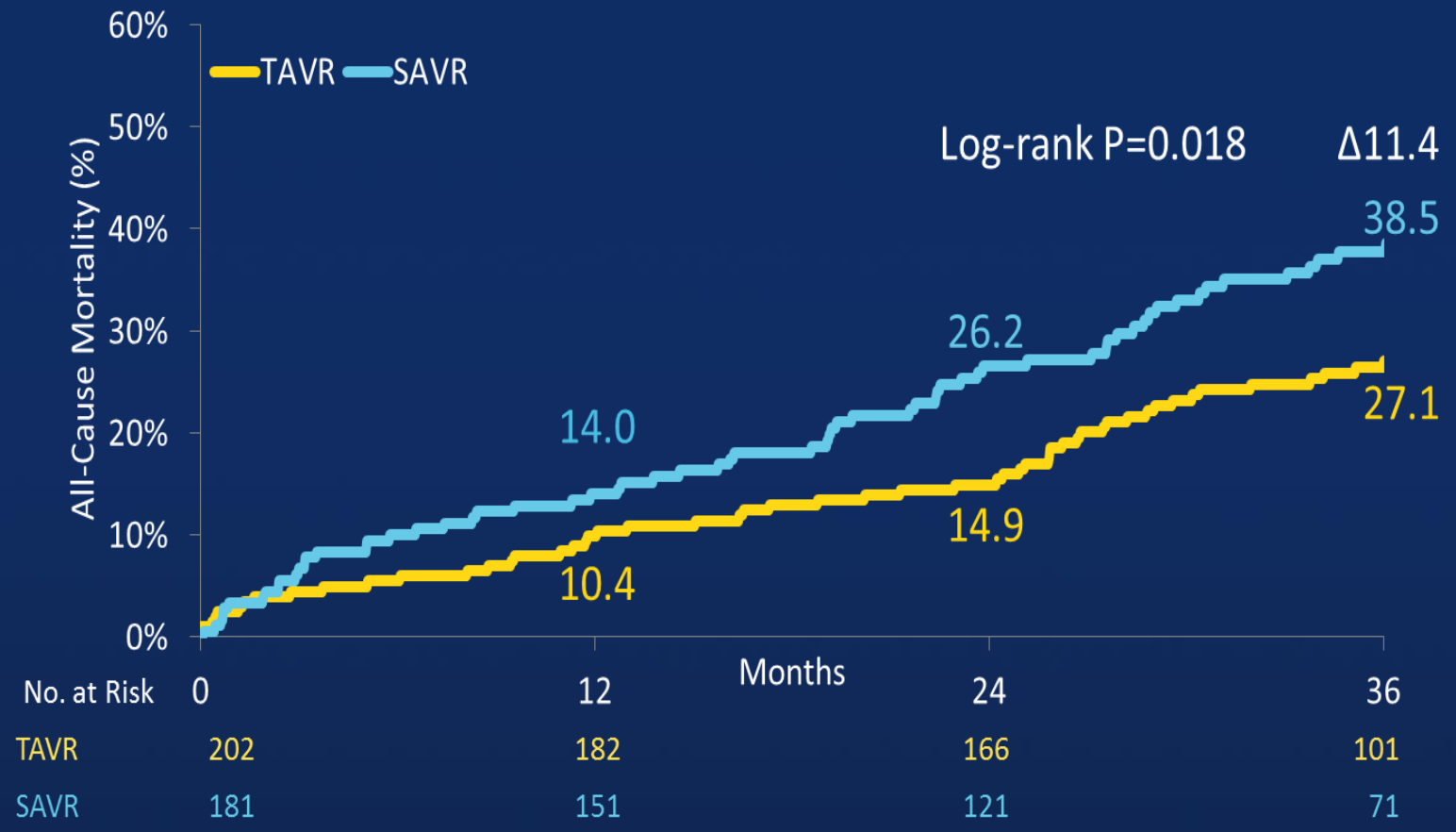
## All-Cause Mortality




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

# CoreValve US Pivotal Trial– 3 year result

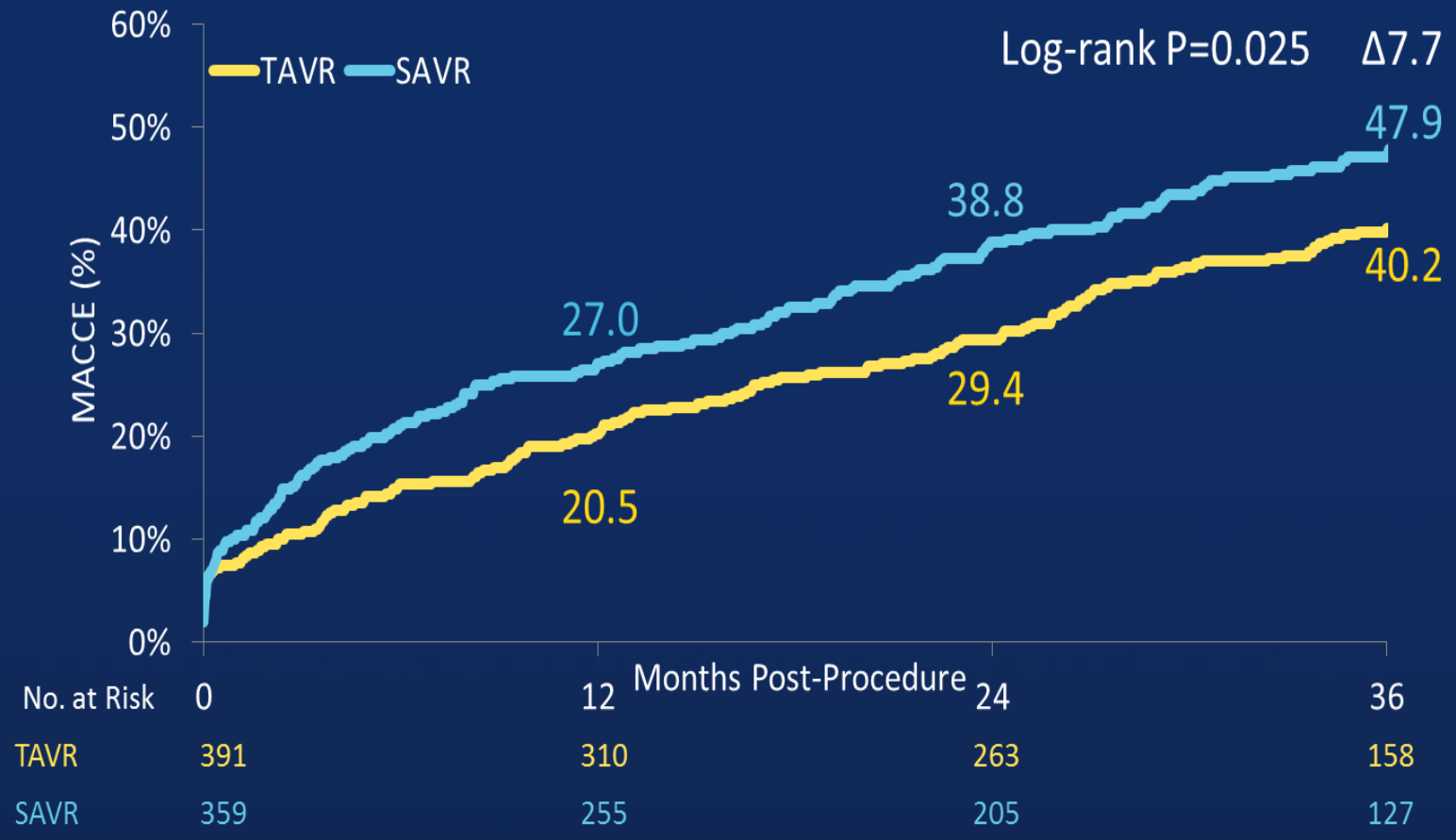
## All-Cause Mortality – STS ≤ 7%




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)*

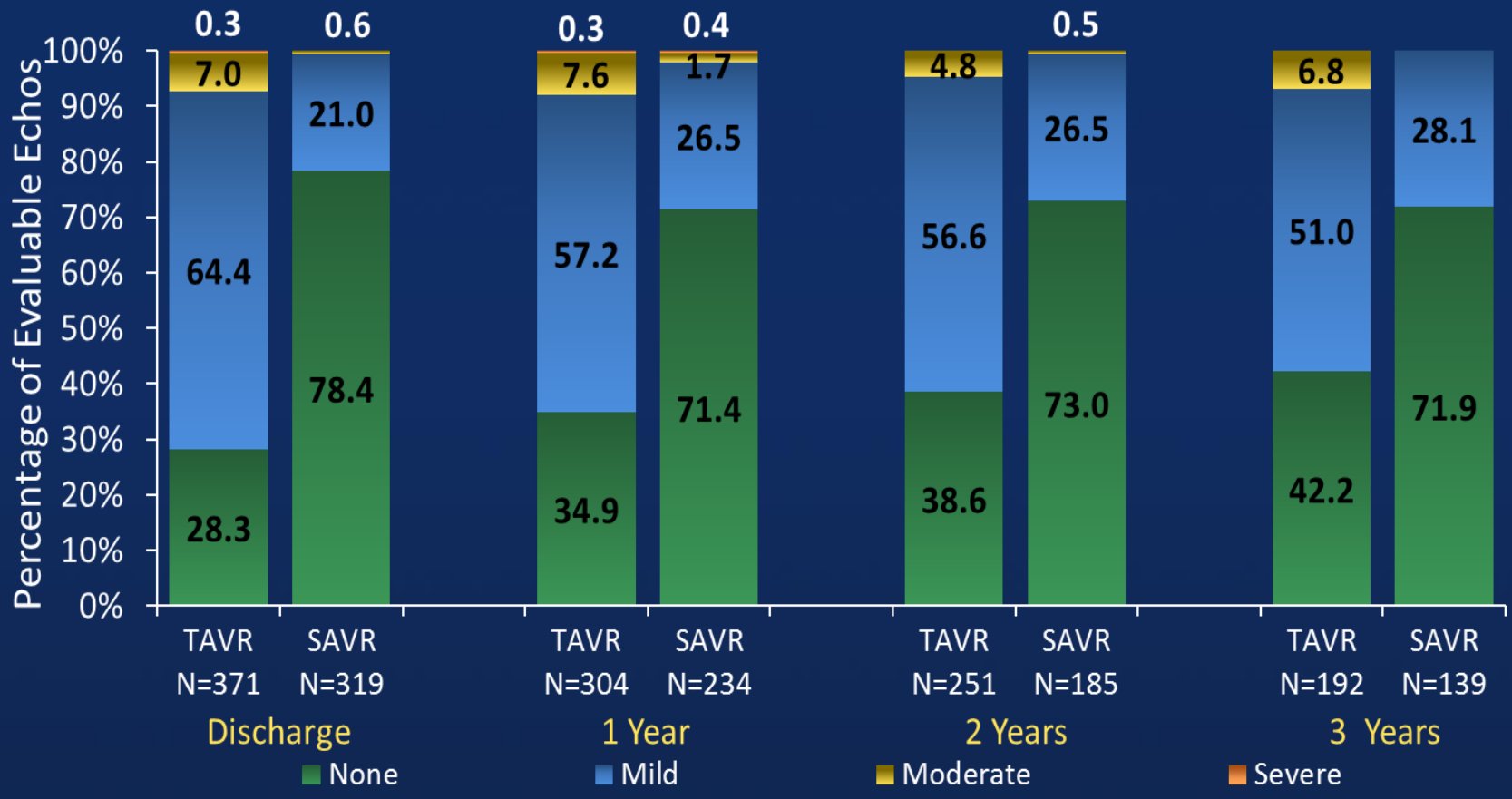
Mean AV Gradients for Patients With >50% Increase From 1 Month to 3 Years


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)*

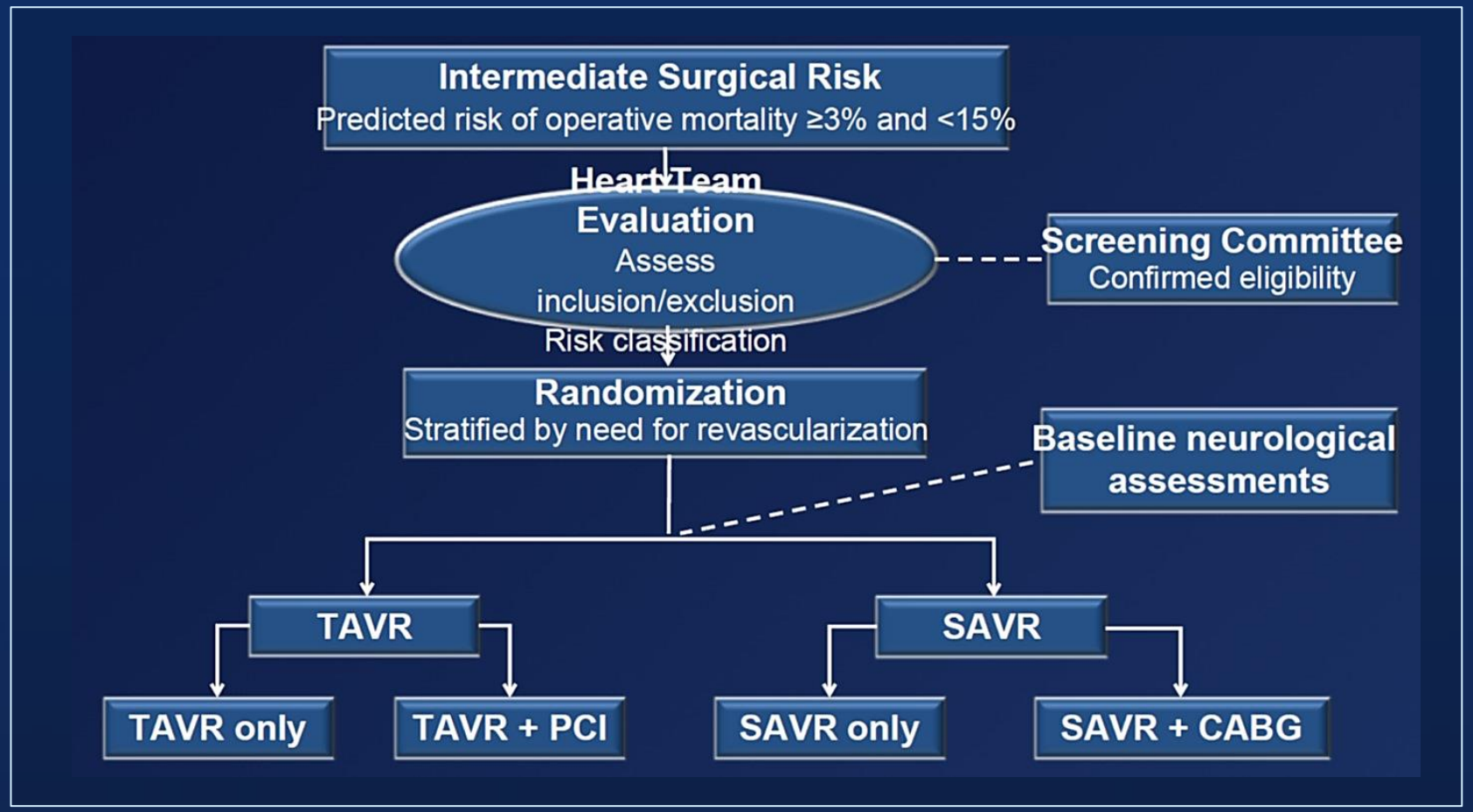
Significantly less AR with SAVR vs. TAVR at Each Time Point (P<0.001)




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

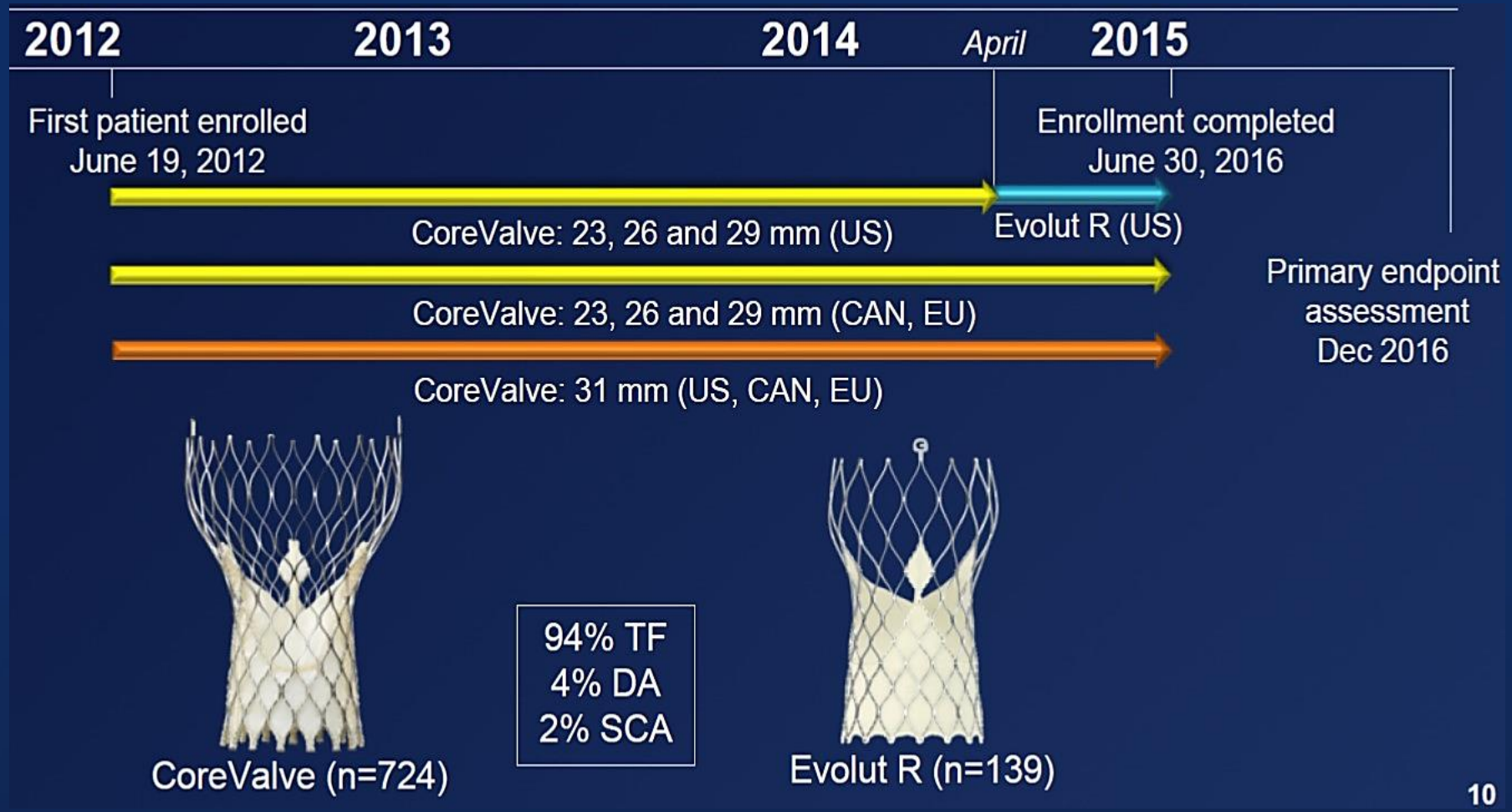
# SURTAVI TRIAL

# Trial Design



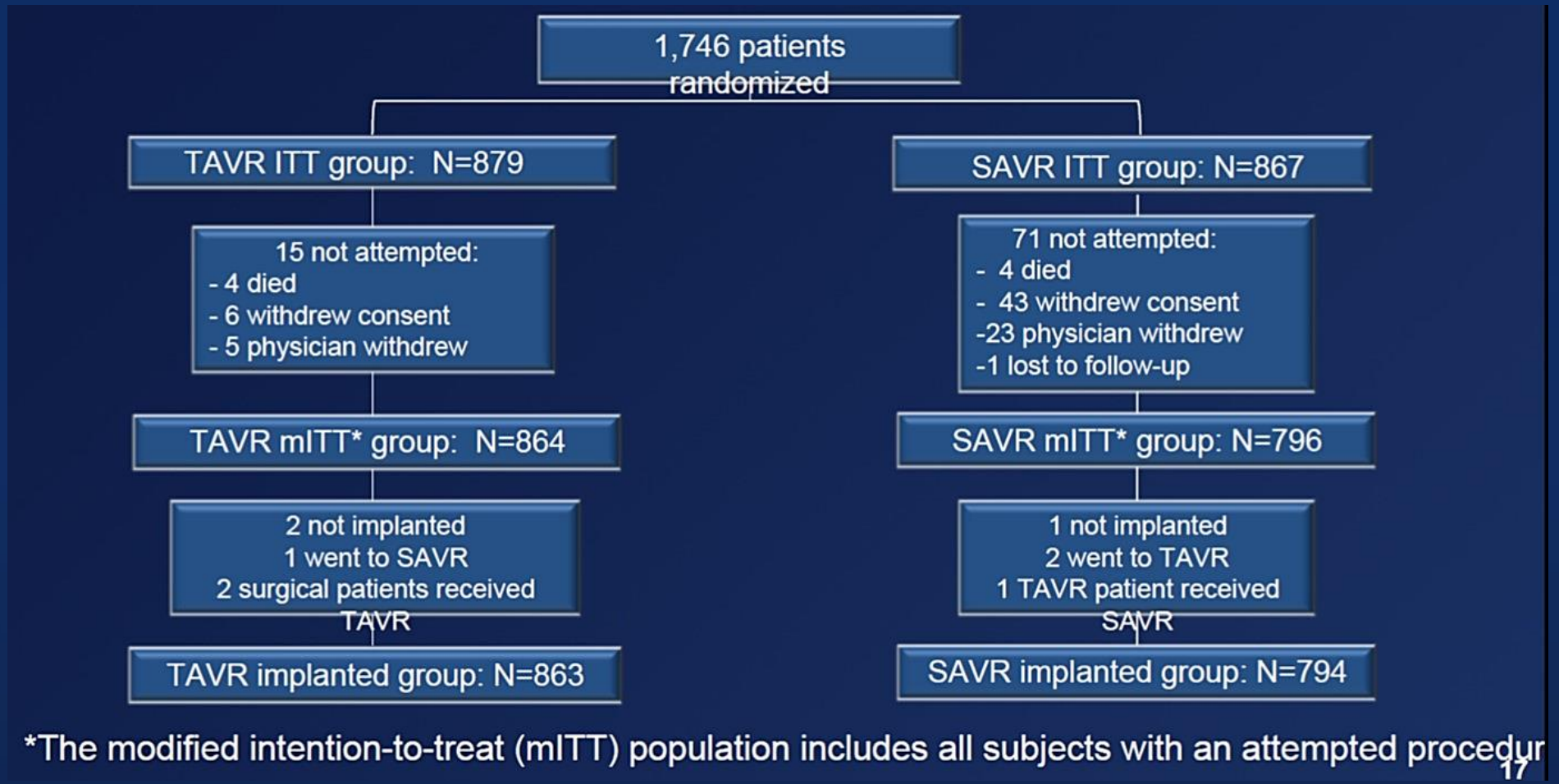

MJ Reardon et al. N Eng J Med. March 17, 2017

# Study Timeline



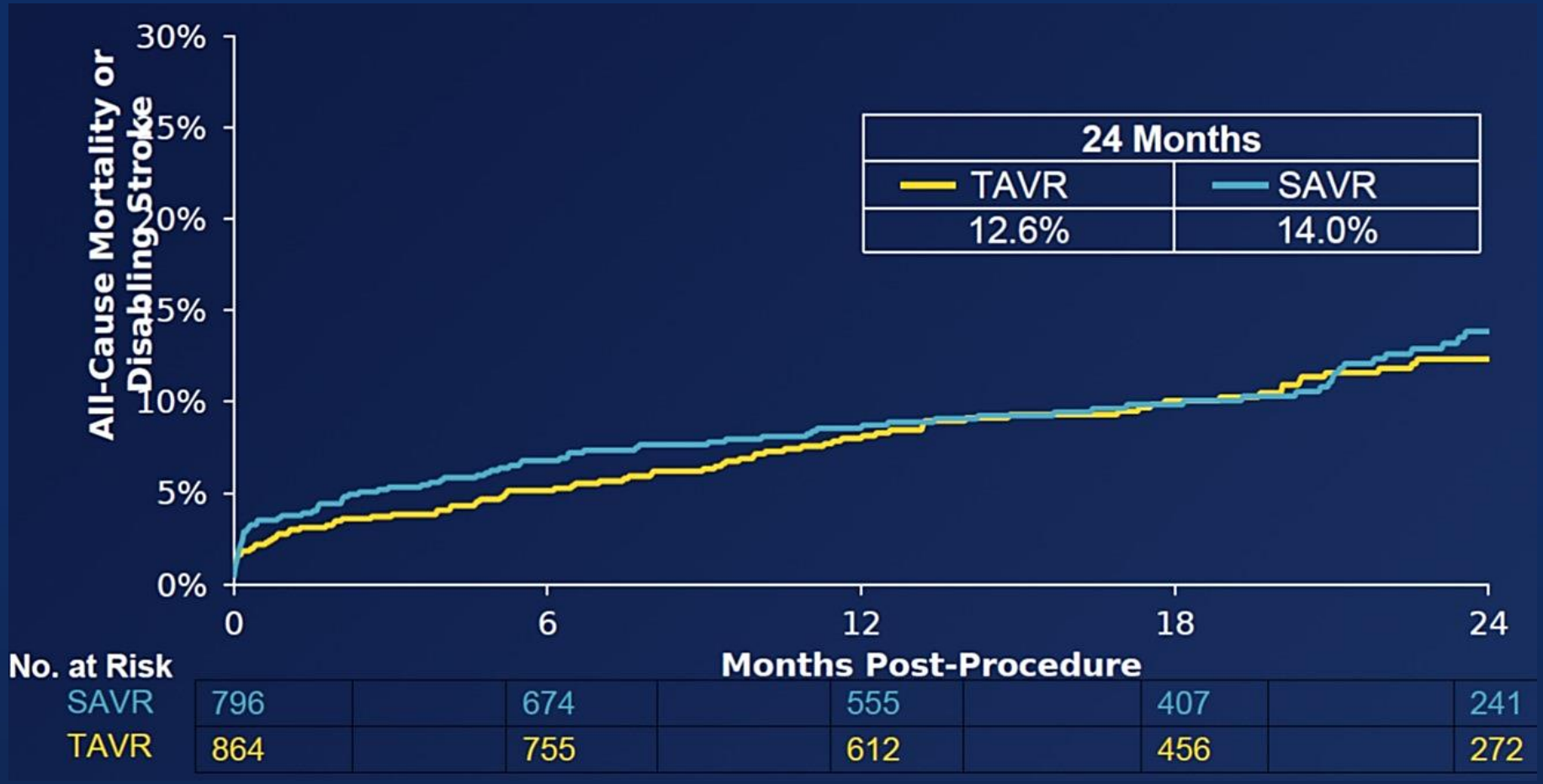

MJ Reardon et al. N Eng J Med. March 17, 2017

# Patient Flow



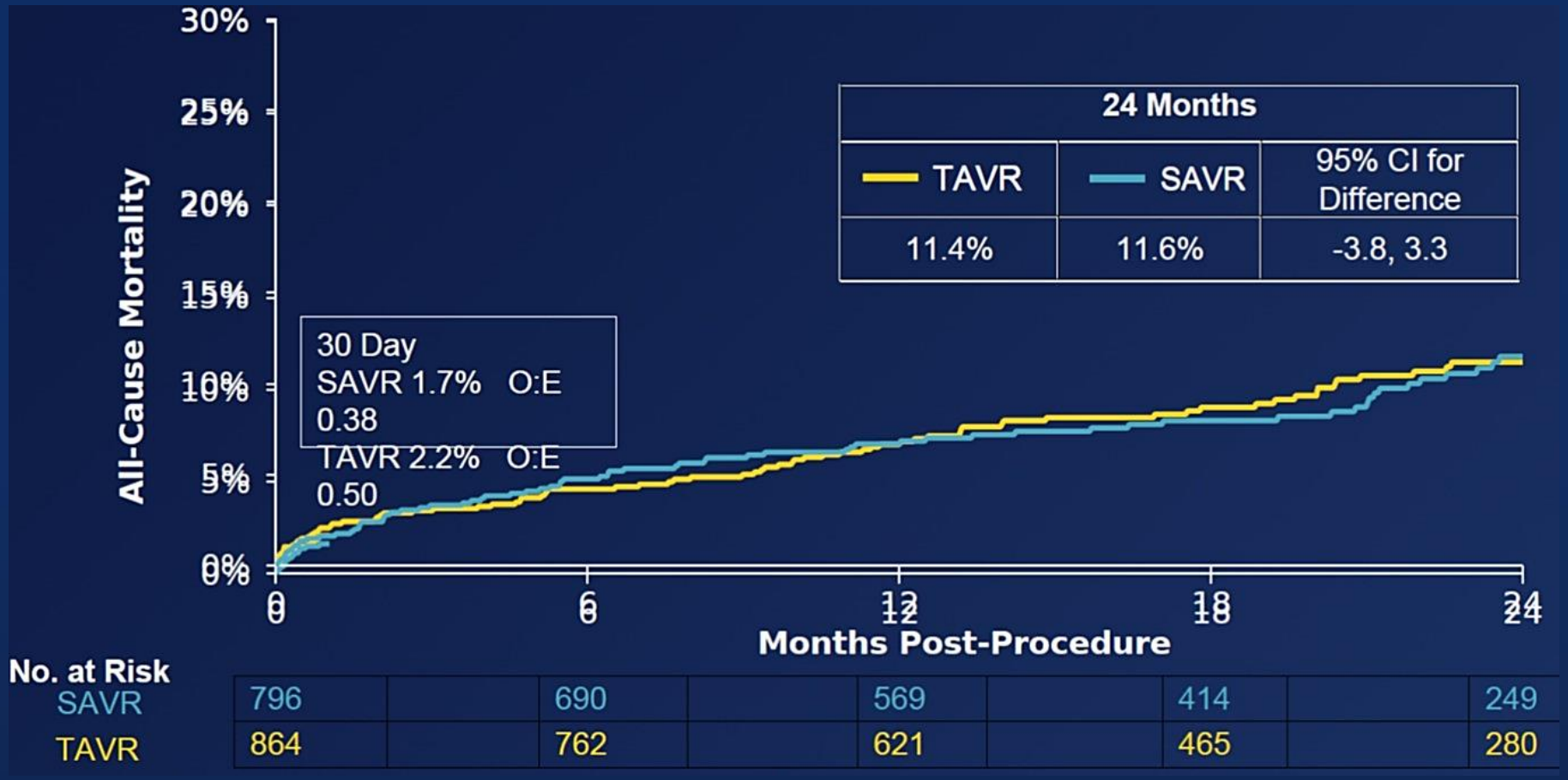

MJ Reardon et al. N Eng J Med. March 17, 2017

# All-Cause Mortality or Disabling Stroke



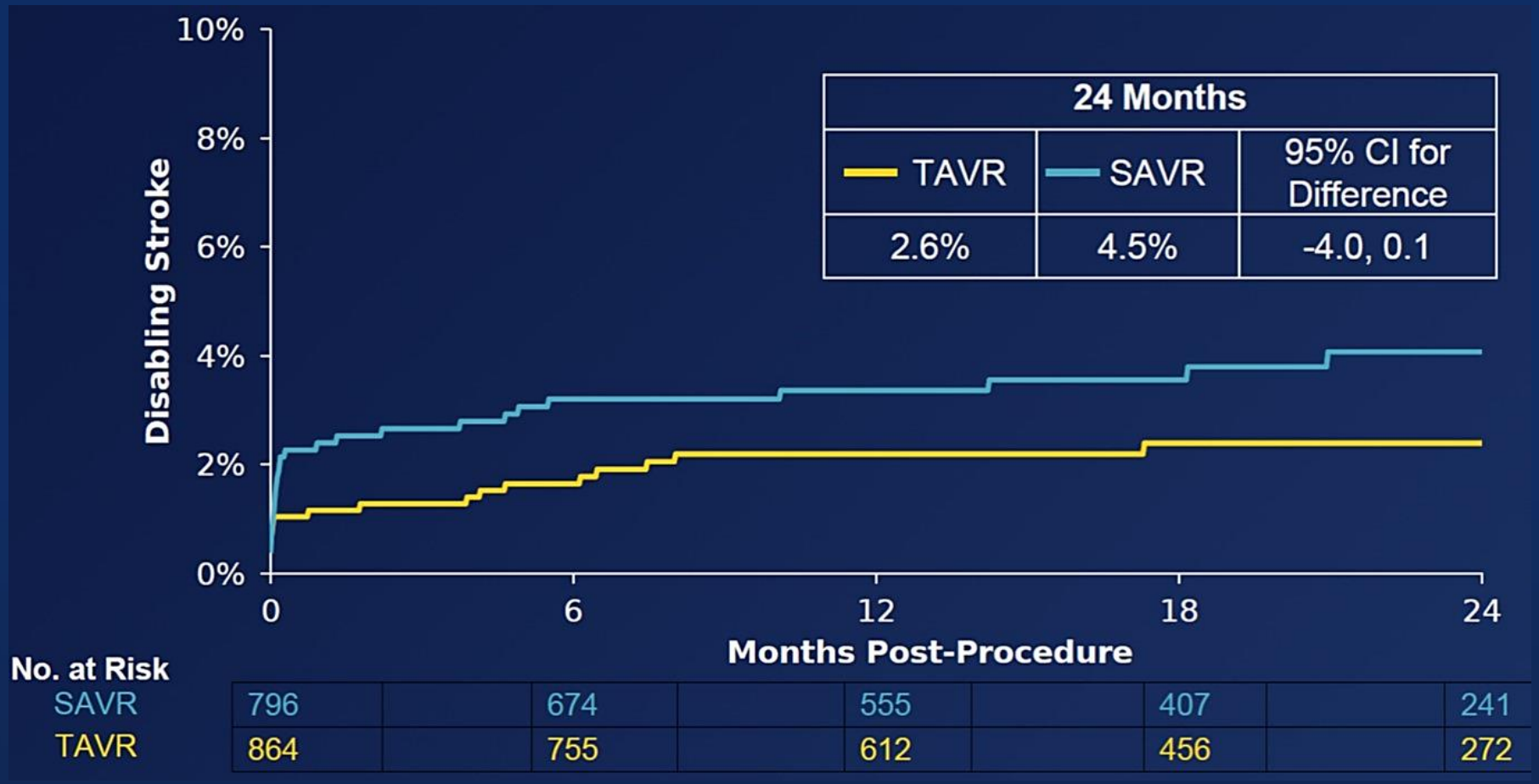

MJ Reardon et al. N Eng J Med. March 17, 2017

# All-Cause Mortality




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

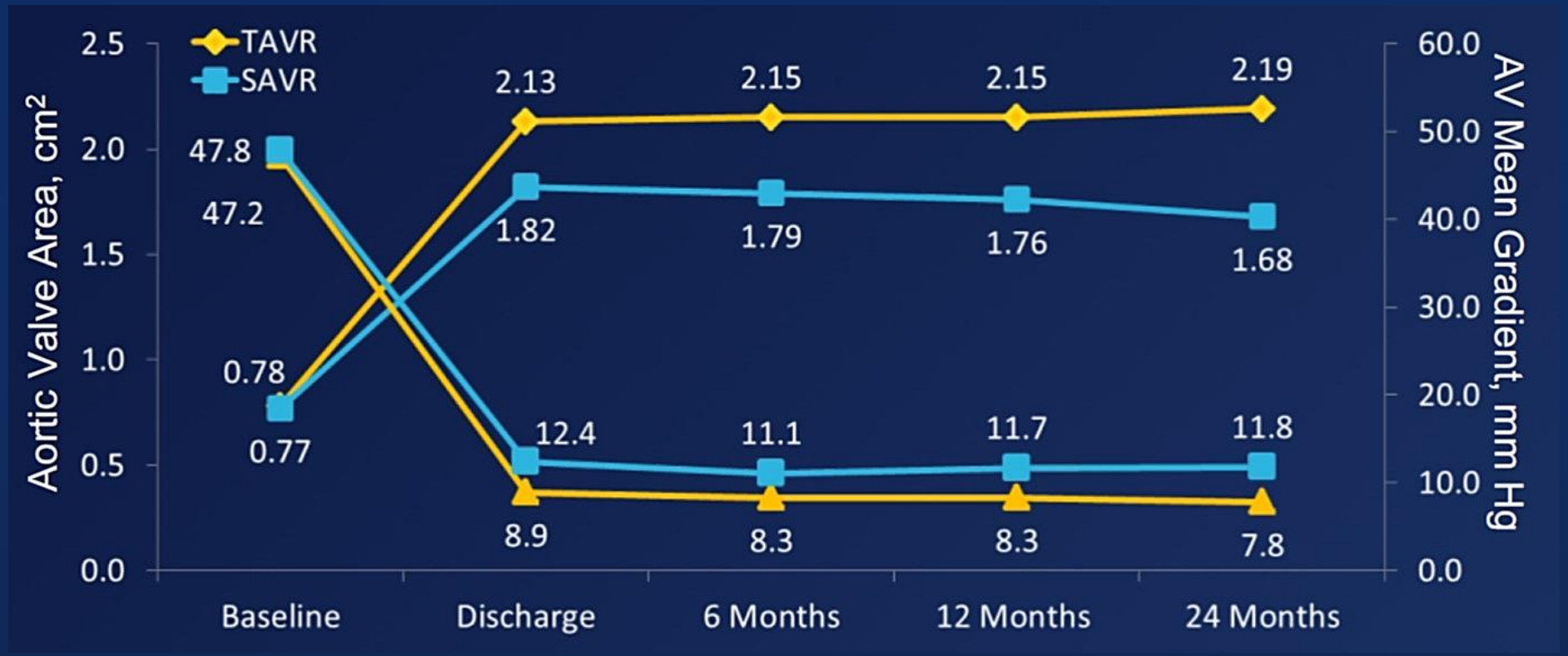
# Disabling Stroke




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

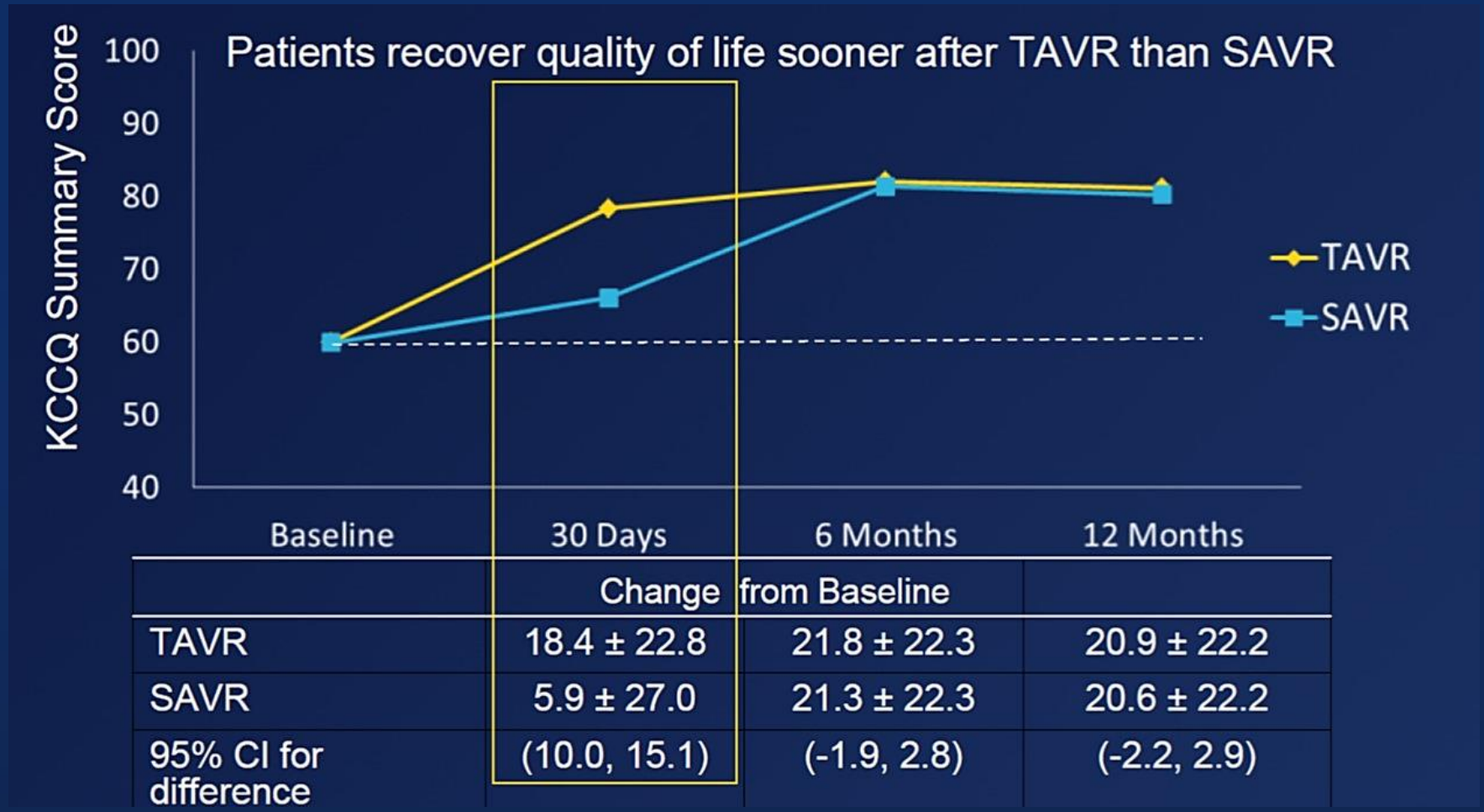
# Hemodynamics

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




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

# 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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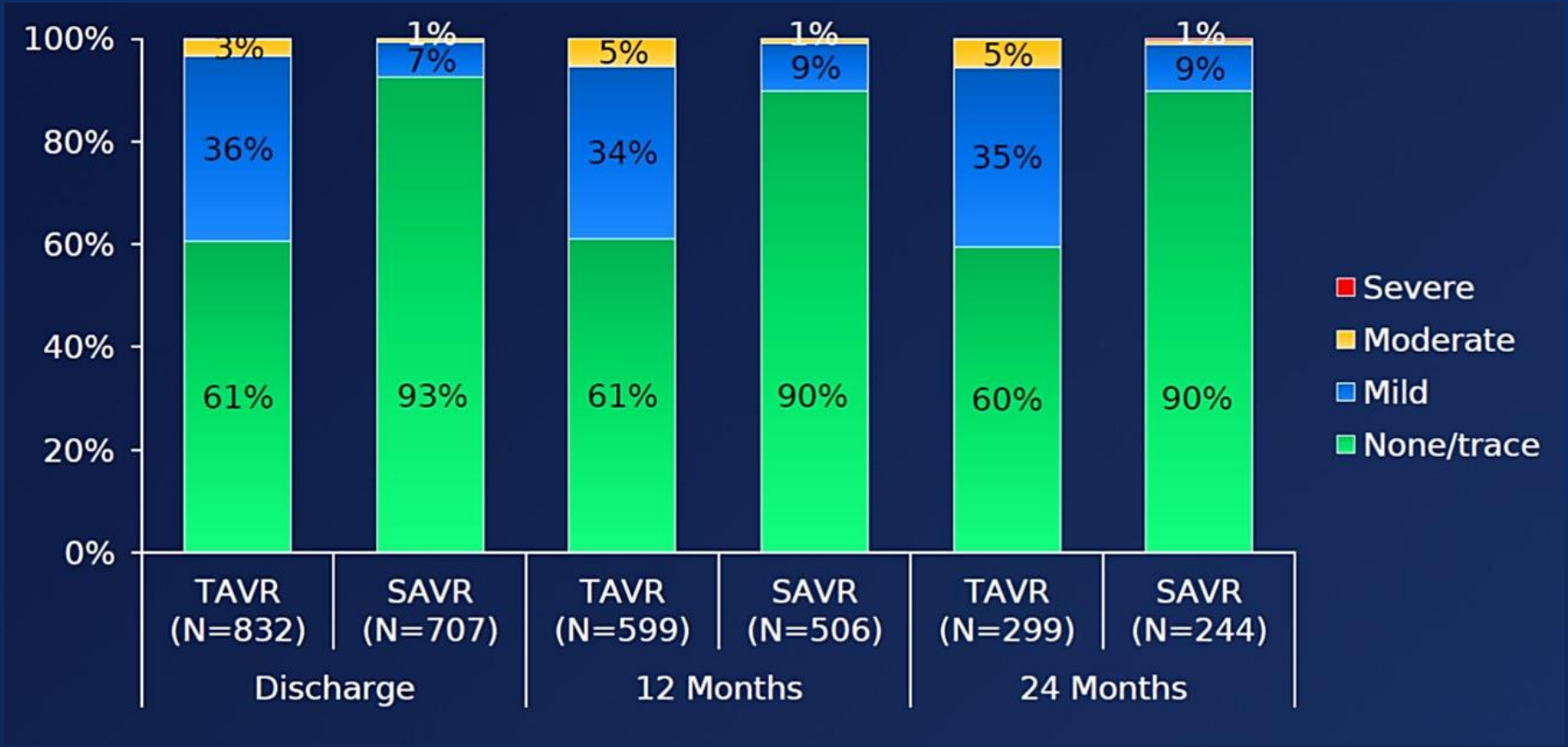
# Total Aortic Regurgitation




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

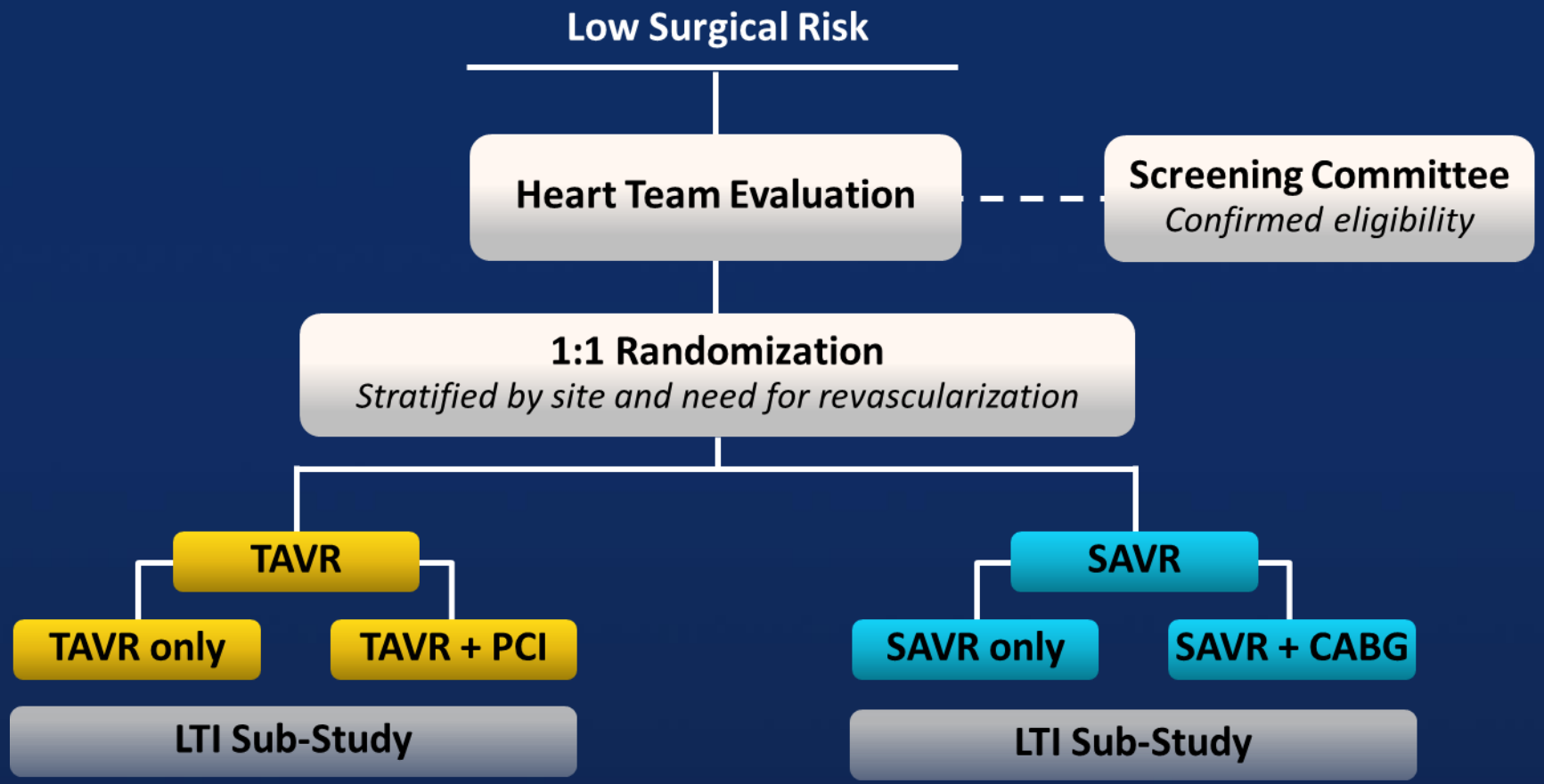
Evolut™ Low Risk Trial

# Evolut Low Risk Trial

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

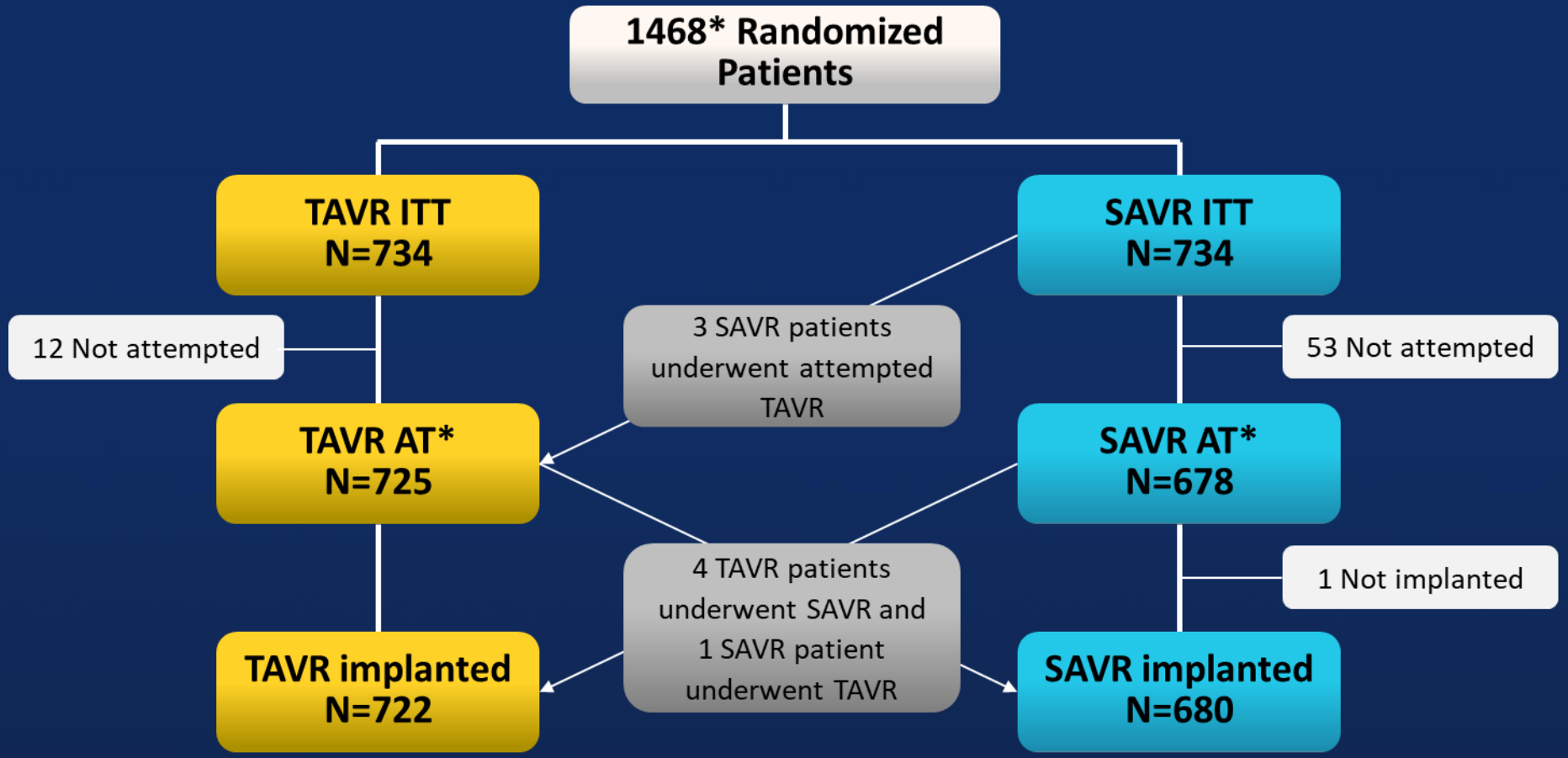
Evolut™ Low Risk Trial

# Study Design



Evolut™ Low Risk Trial

# 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.

Evolut™ Low Risk Trial

# Evolut Low Risk Trial

## 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.

Evolut™ Low Risk Trial

# Evolut Low Risk Trial

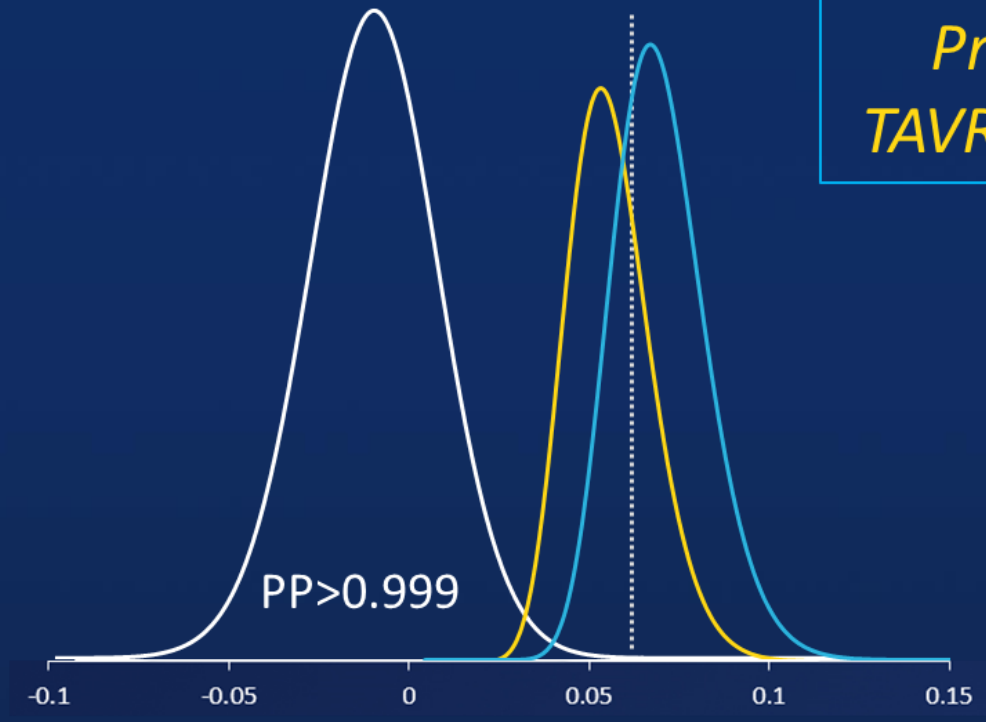
## TAVR Procedural Data

| % | 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 |

Evolut™ Low Risk Trial

# 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)

Evolut™ Low Risk Trial

# 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

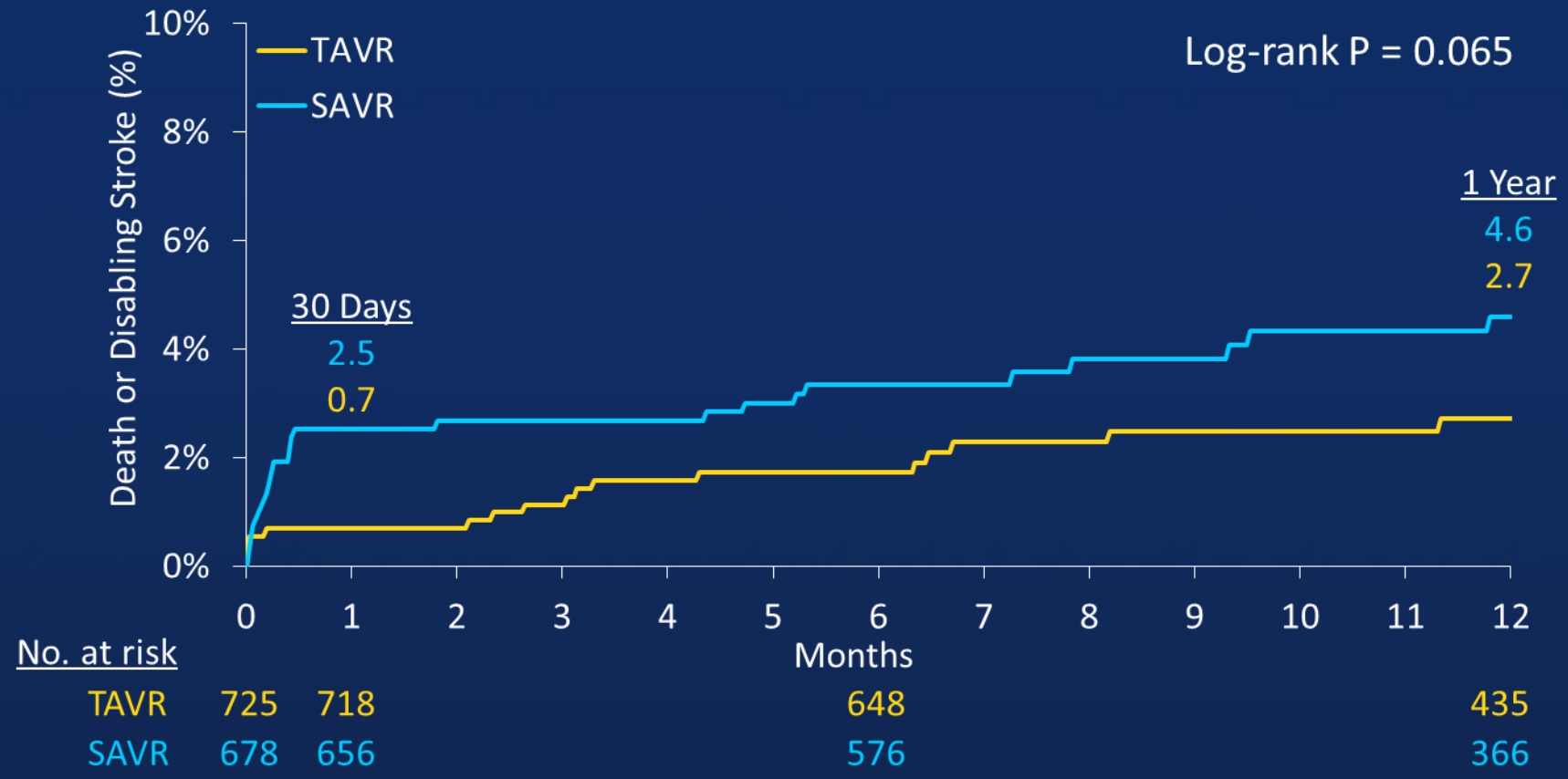
| Bayesian rates as % | TAVR (N=725) | SAVR (N=678) | (95% BCI for Difference) |
|---|---|---|---|
| All-cause mortality or disabling stroke | 2.9 | 4.6 | (-4.0, 0.4) |
| All-cause mortality | 2.4 | 3.0 | (-2.6, 1.3) |
| Cardiovascular mortality | 1.7 | 2.6 | (-2.7, 0.7) |
| All stroke | 4.1 | 4.3 | (-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

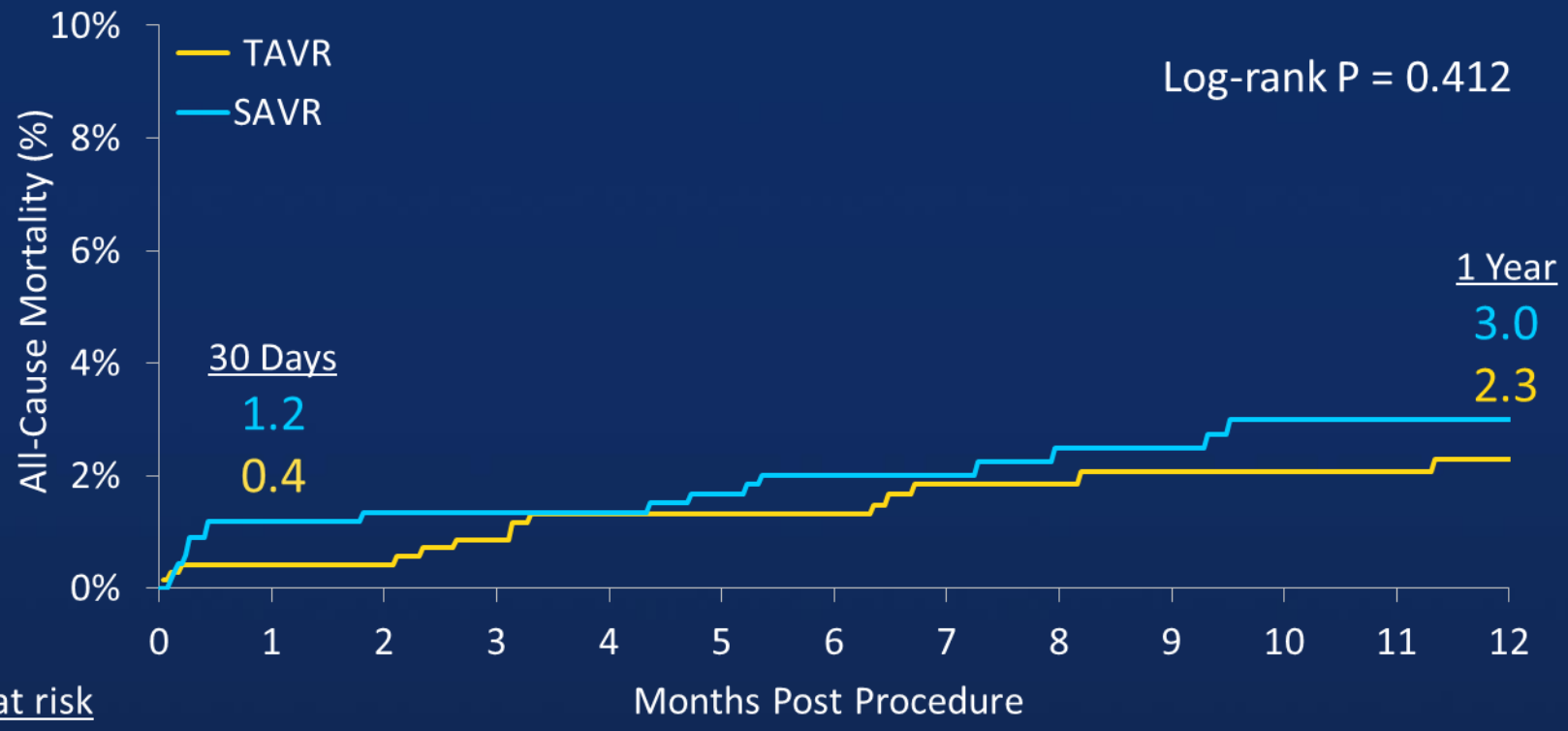
## K-M All-Cause Mortality or Disabling Stroke at 1 Year



Evolut™ Low Risk Trial

# Evolut Low Risk Trial

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

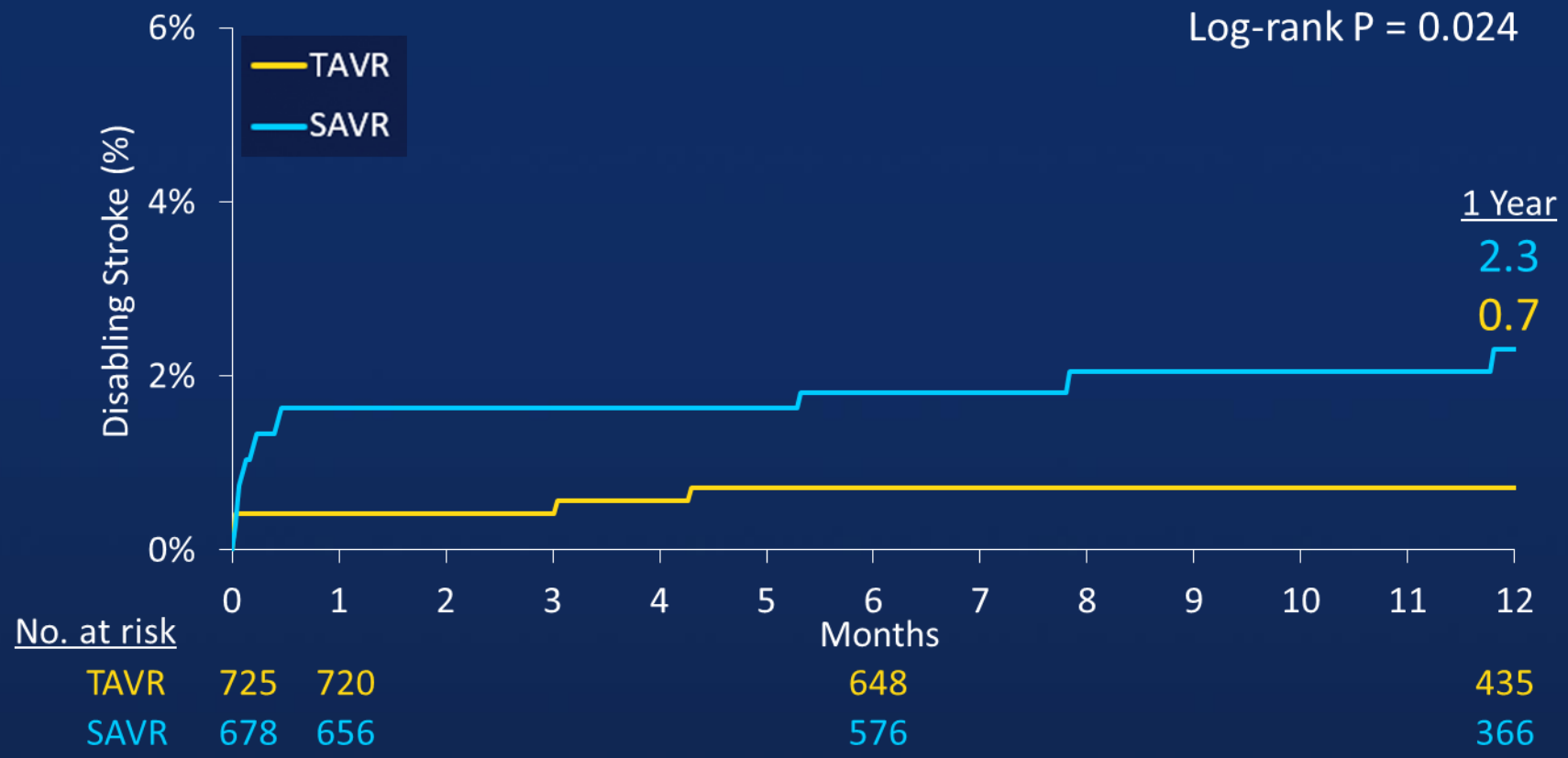



No. at risk

| | | | | |
|---|---|---|---|---|
| TAVR | 725 | 720 | 651 | 435 |
| SAVR | 678 | 665 | 583 | 373 |

# Evolut Low Risk Trial

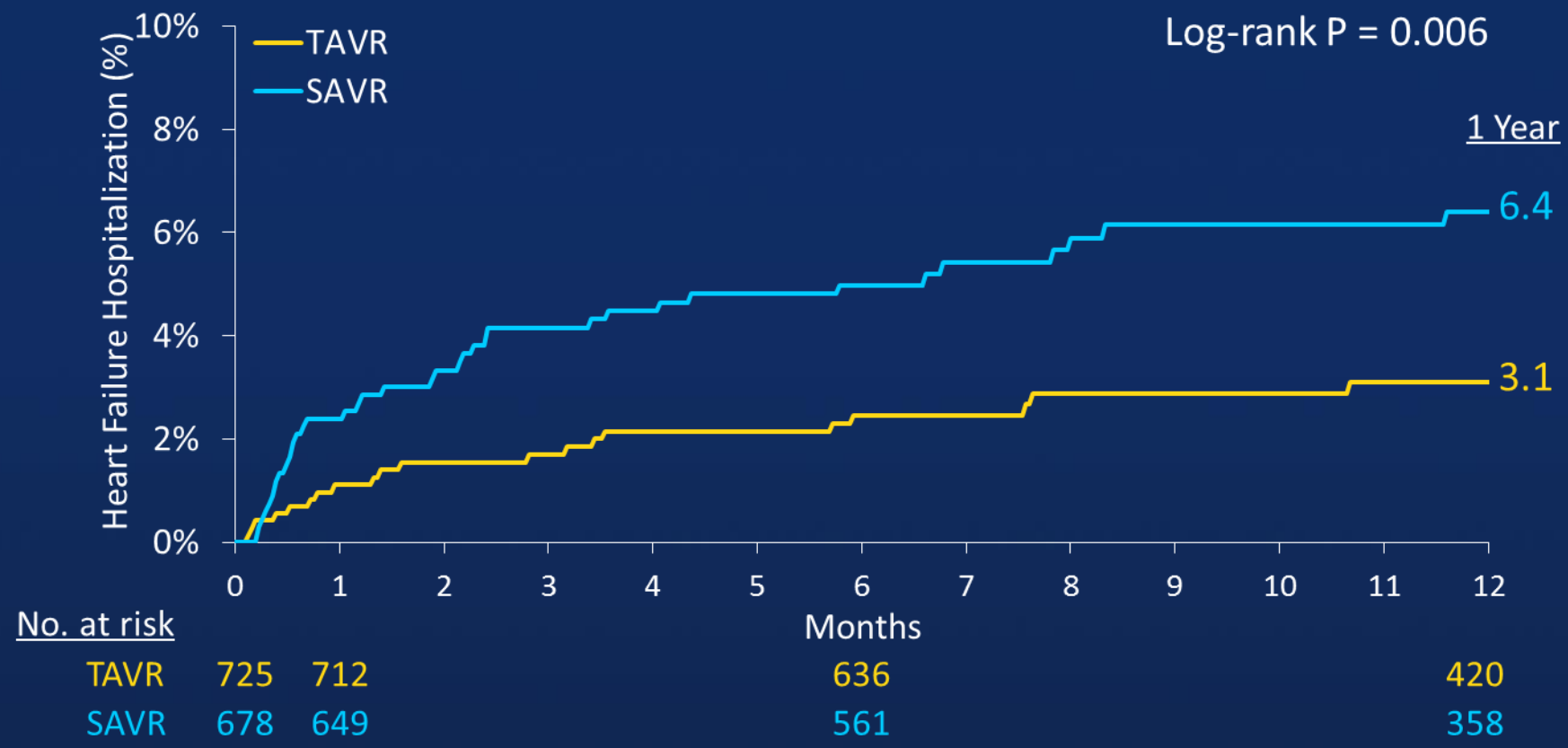
## K-M Disabling Stroke at 1 Year



Evolut™ Low Risk Trial

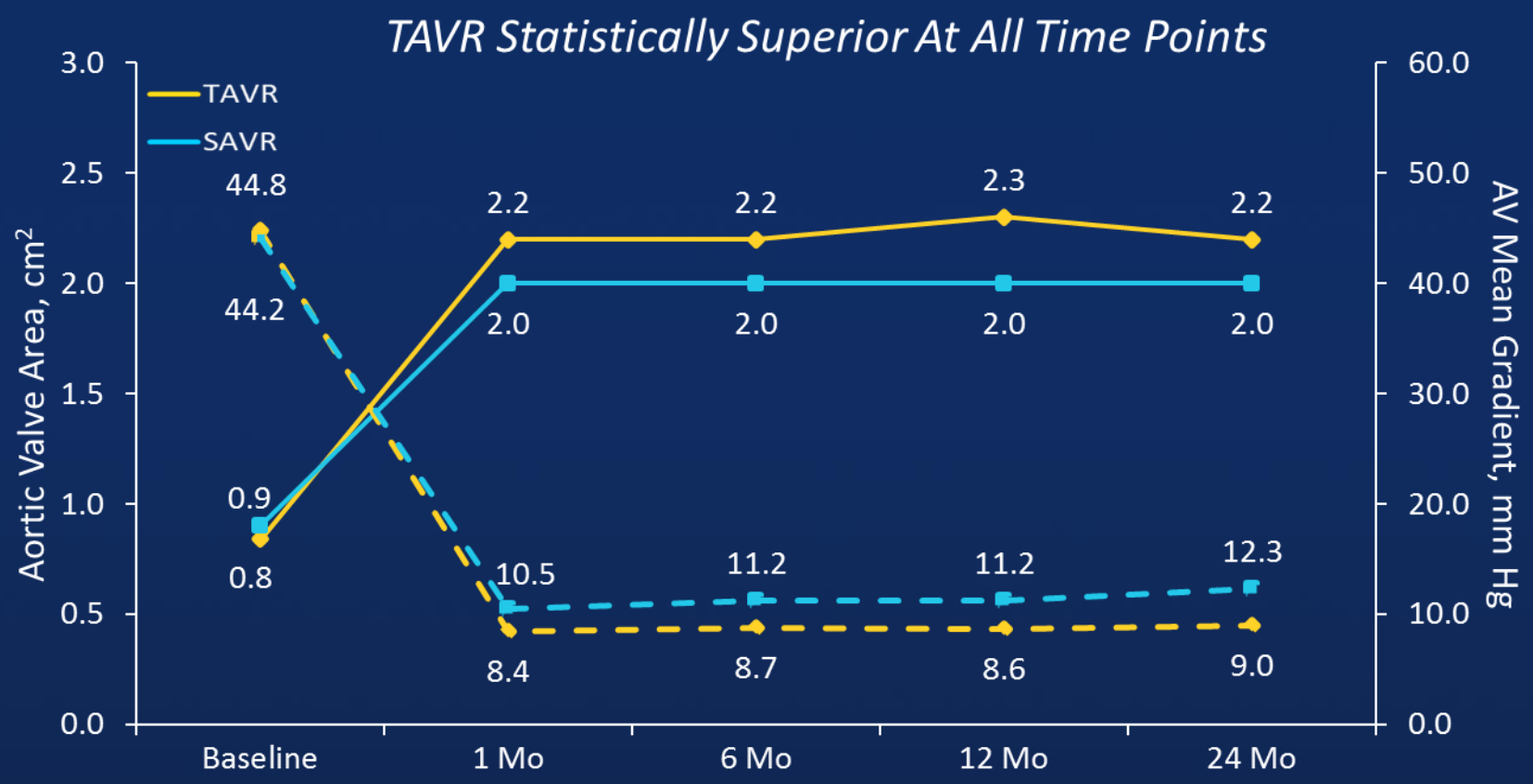
# Evolut Low Risk Trial

## K-M Heart Failure Hospitalization at 1 Year



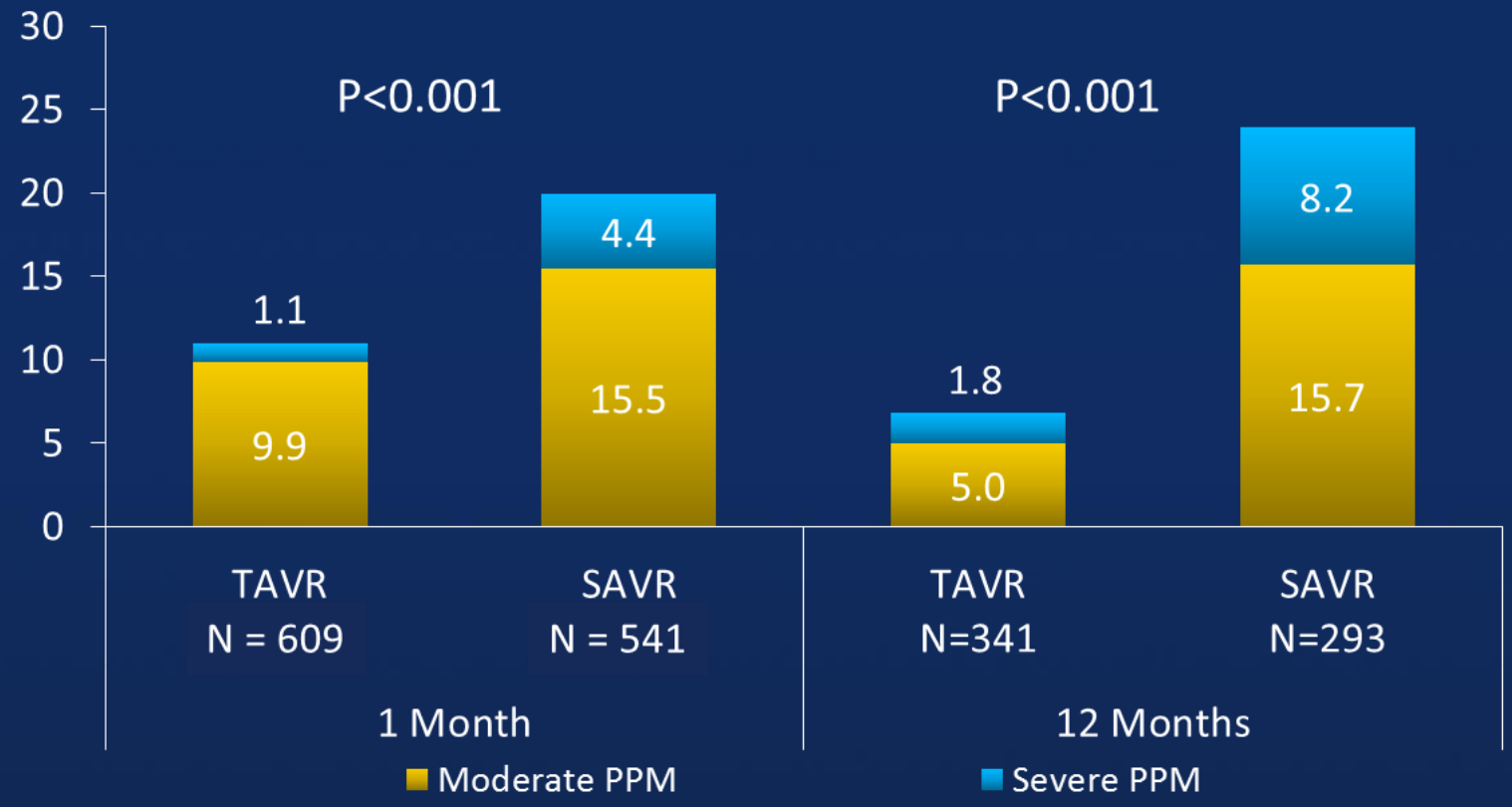
Evolut™ Low Risk Trial

# Valve Hemodynamics




Implanted population. Core lab assessments.

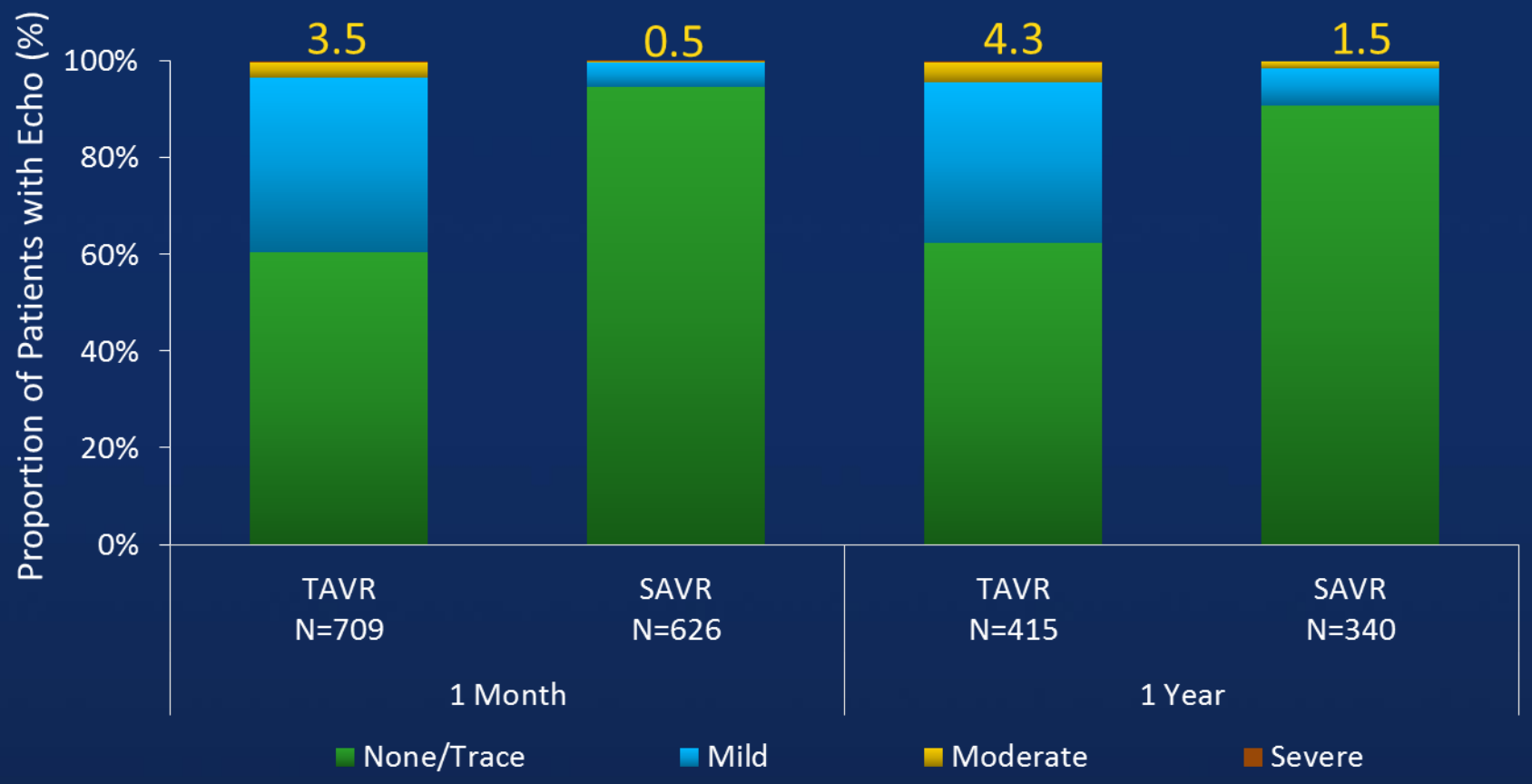
# Prosthesis-Patient Mismatch




Implant population. Core lab assessments.

# Total Aortic Valve Regurgitation

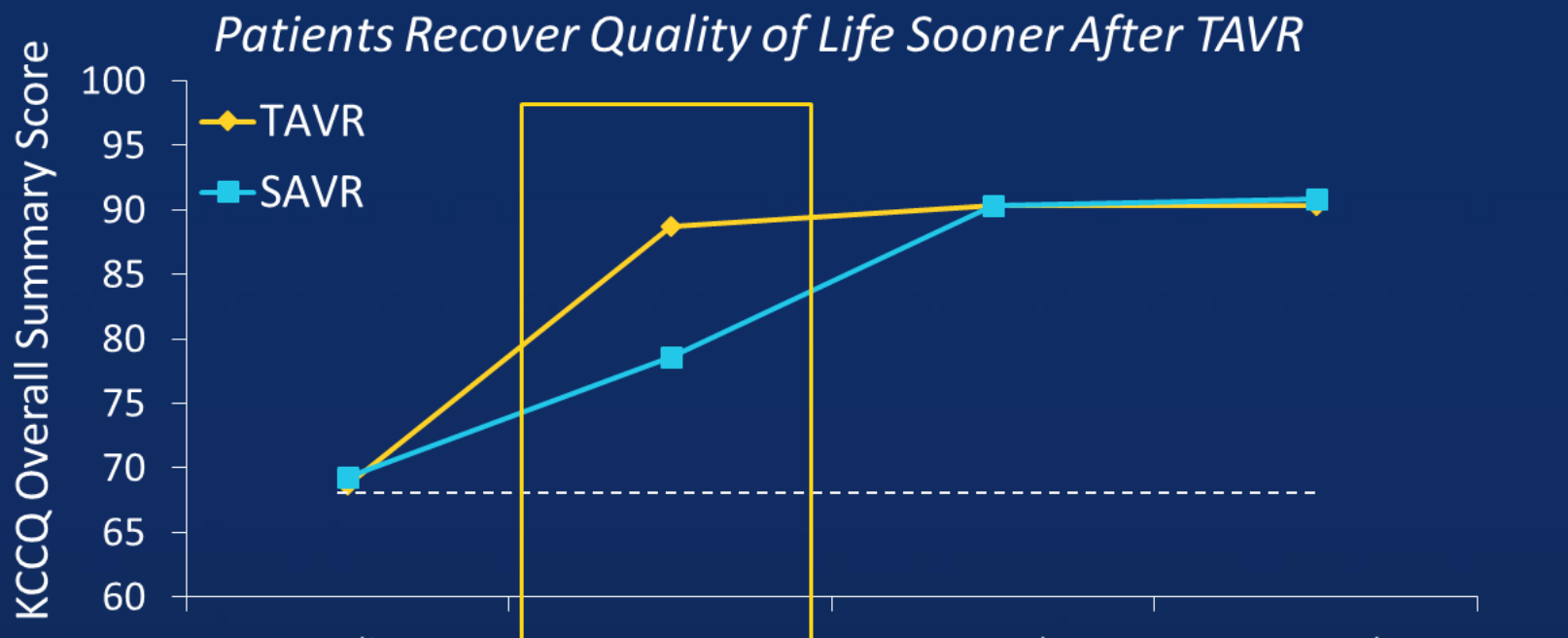
Evolut™ Low Risk Trial




Implant population. Core lab assessments.

Evolut™ Low Risk Trial

# KCCQ Summary Score




| | | 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

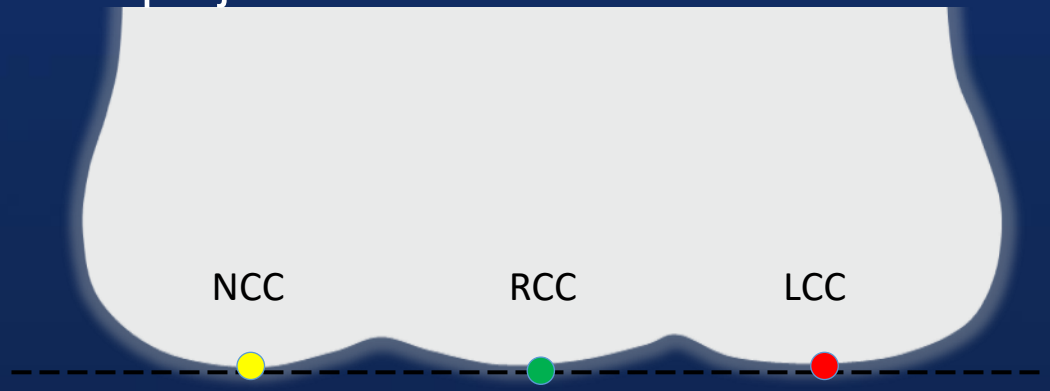
# Pre-Procedure CT Planning

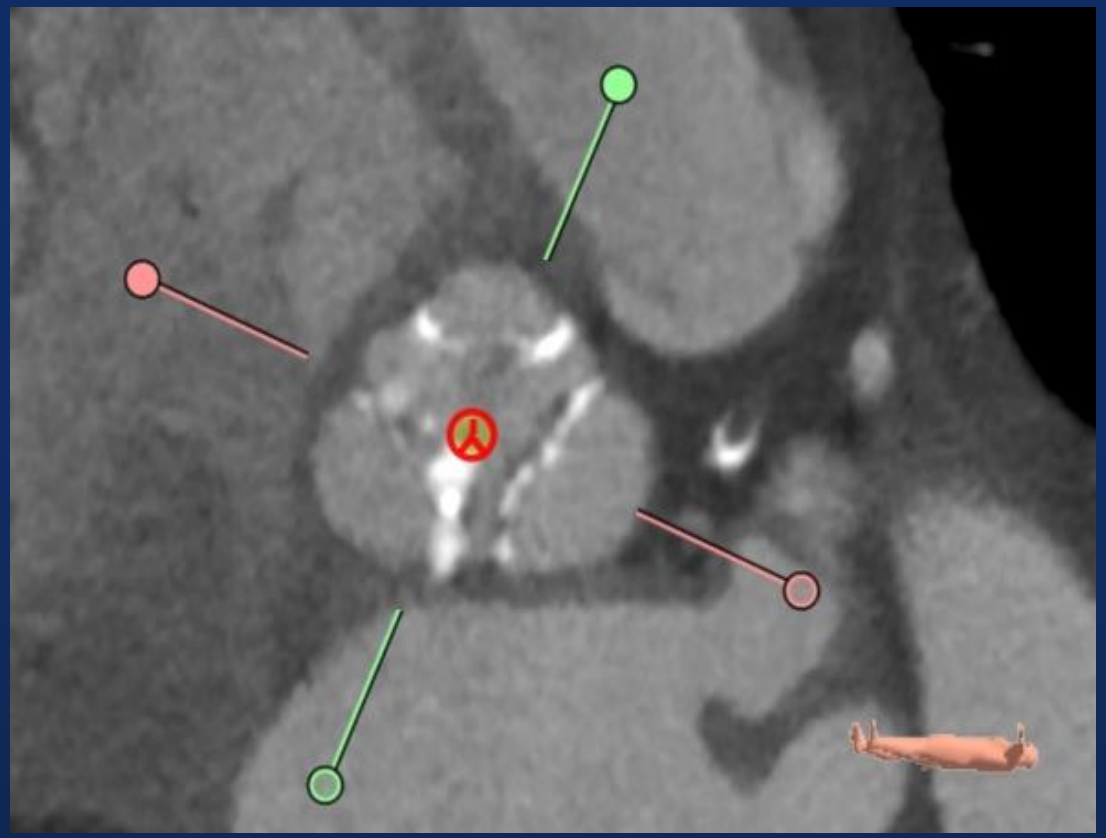
## BASAL ANNULAR PLANE

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.

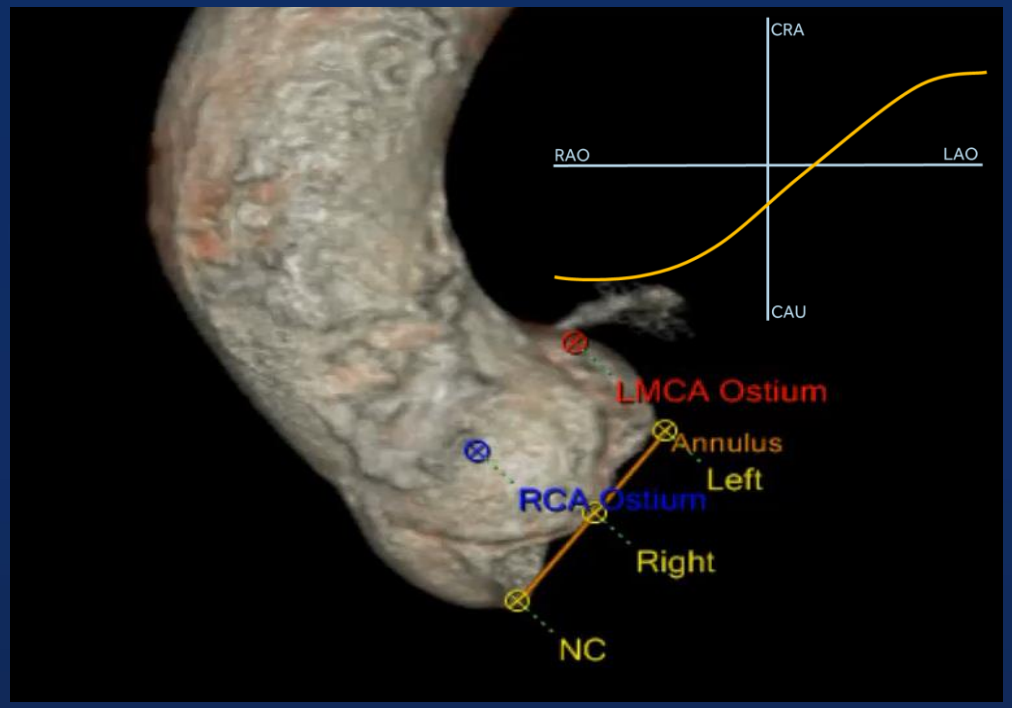
- Centering markers on the cusps is critical for CT determination of overlap imaging projections.



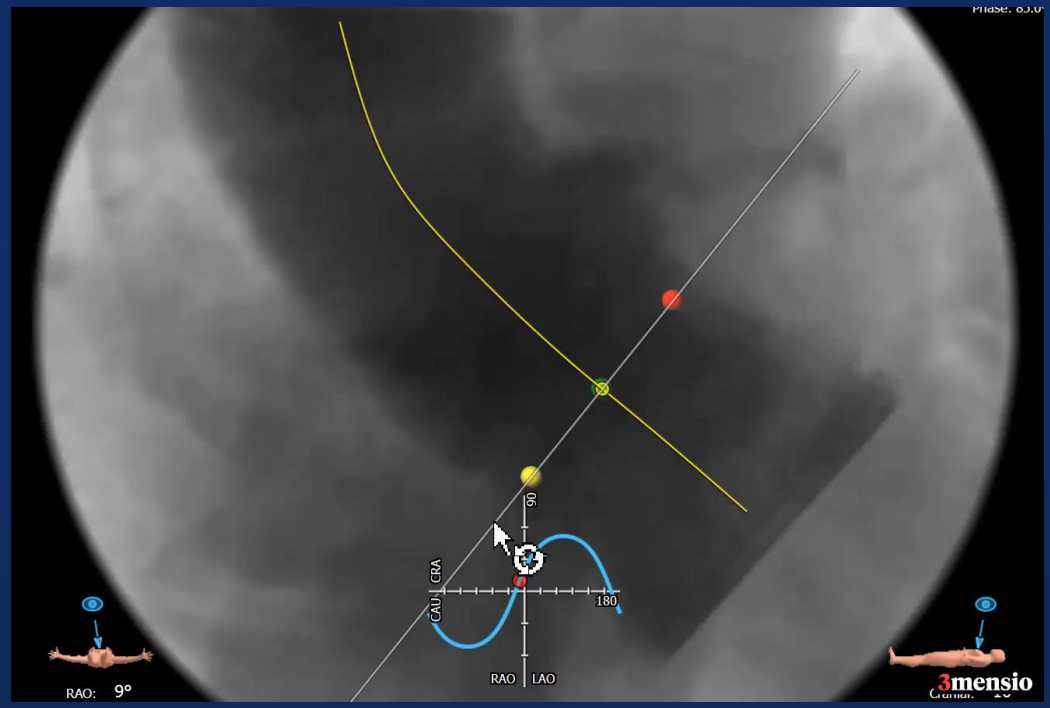



# Determine Cusp Overlap Imaging Projections

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.



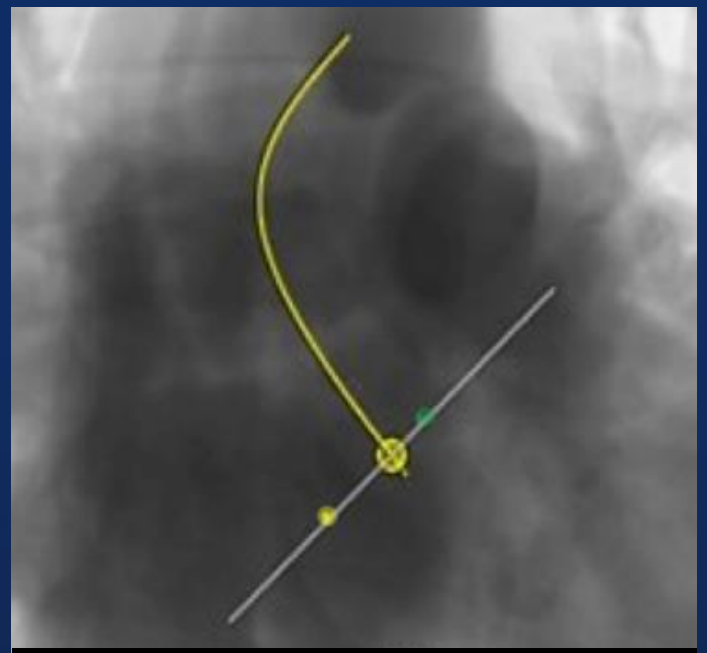

In a long axis view, determine cusp overlap projection by moving along S-curve until RCC and LCC overlap.

# Pre-Procedure CT Planning

## NEAR OVERLAP VIEW EXAMPLE

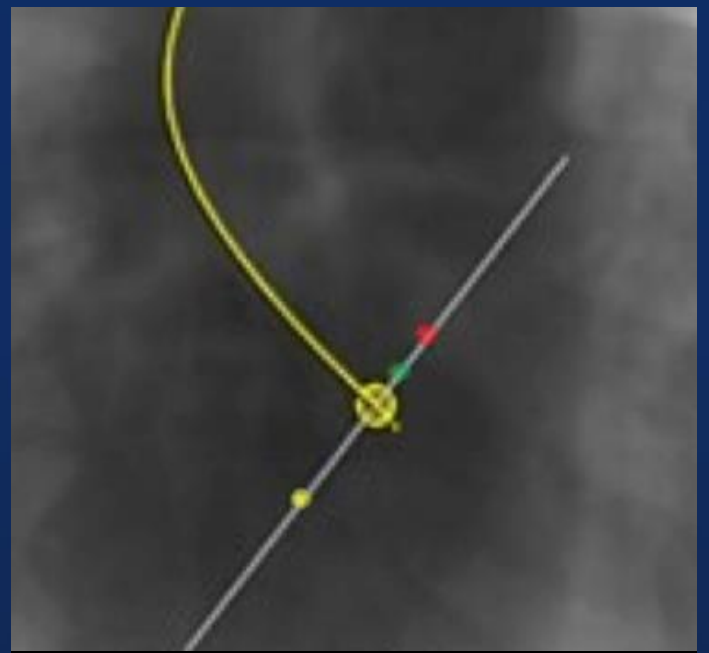
If the cusp overlap imaging projection is unattainable due to patient body habitus and/or equipment limitations, move along S-curve to a near cusp overlap view.

Overlap View



RAO 13˚, Caudal 42˚

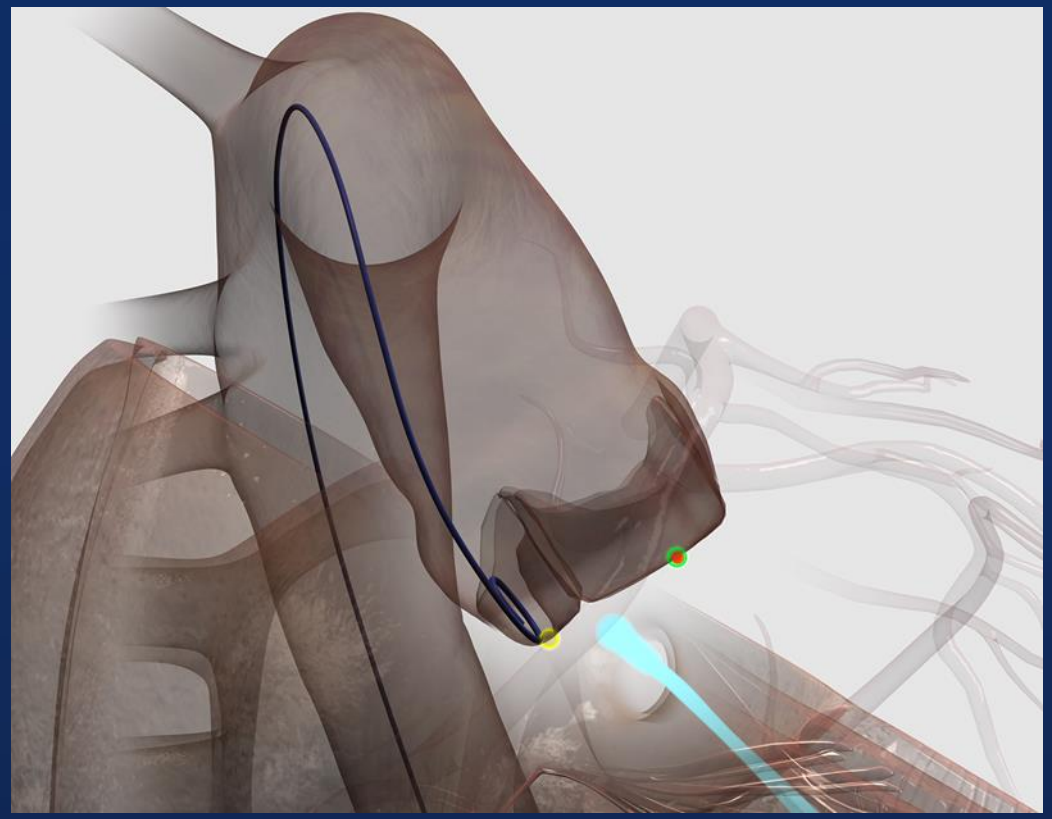
Near Overlap View



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]:

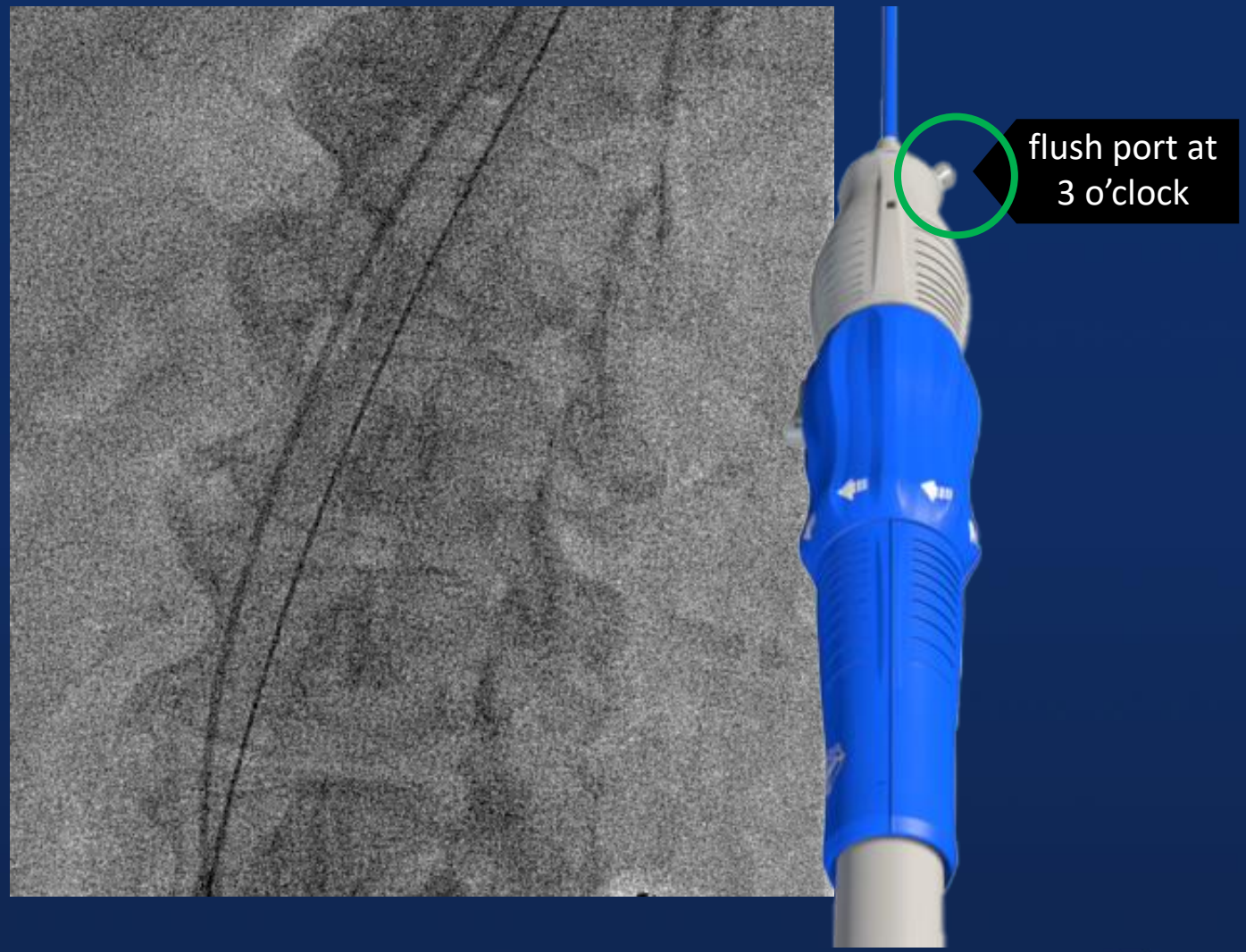
- This error results in TAV appearing higher than actual depth.
- An approximate error of 1 mm in depth is introduced for each 10° movement in the LAO or Caudal directions.

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.

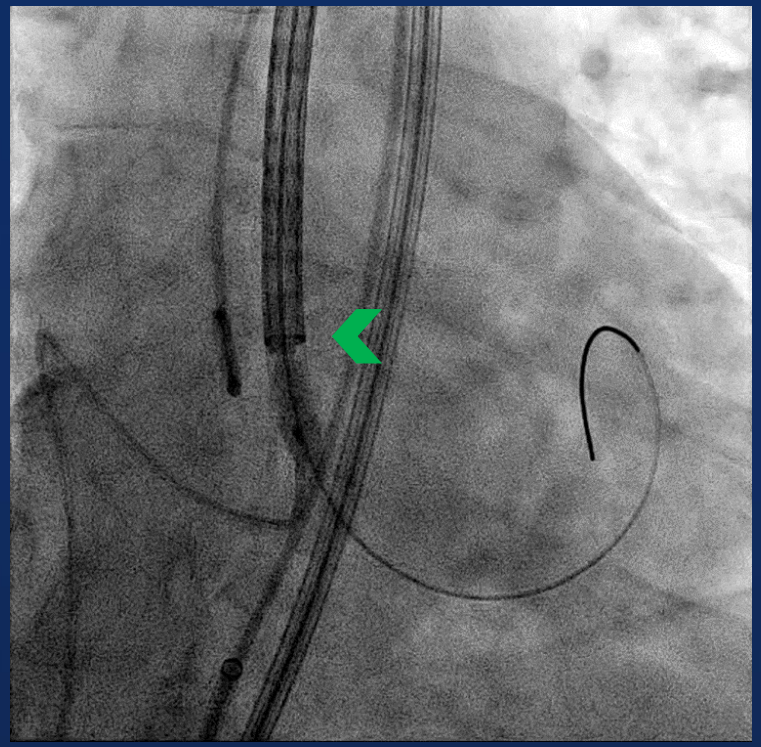
- 3 o'clock flush port orientation is reported to be associated with higher rates of commissural alignment between the TAV and native anatomy.[1]
- Commissural alignment may help facilitate future coronary access.



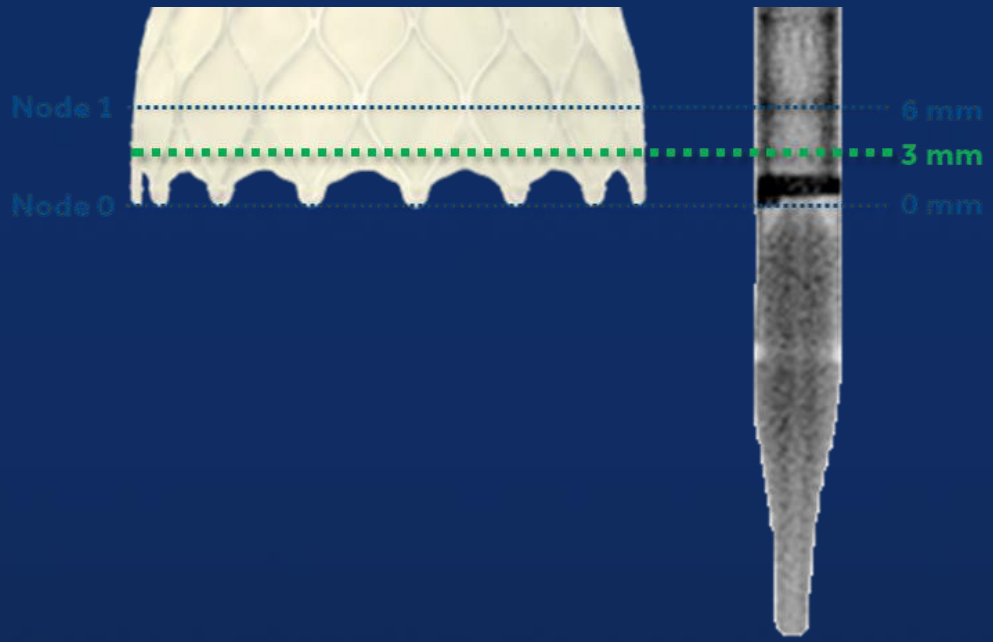

1. Tang et al. JACC: Cardiovascular Interventions, 2020.

# 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

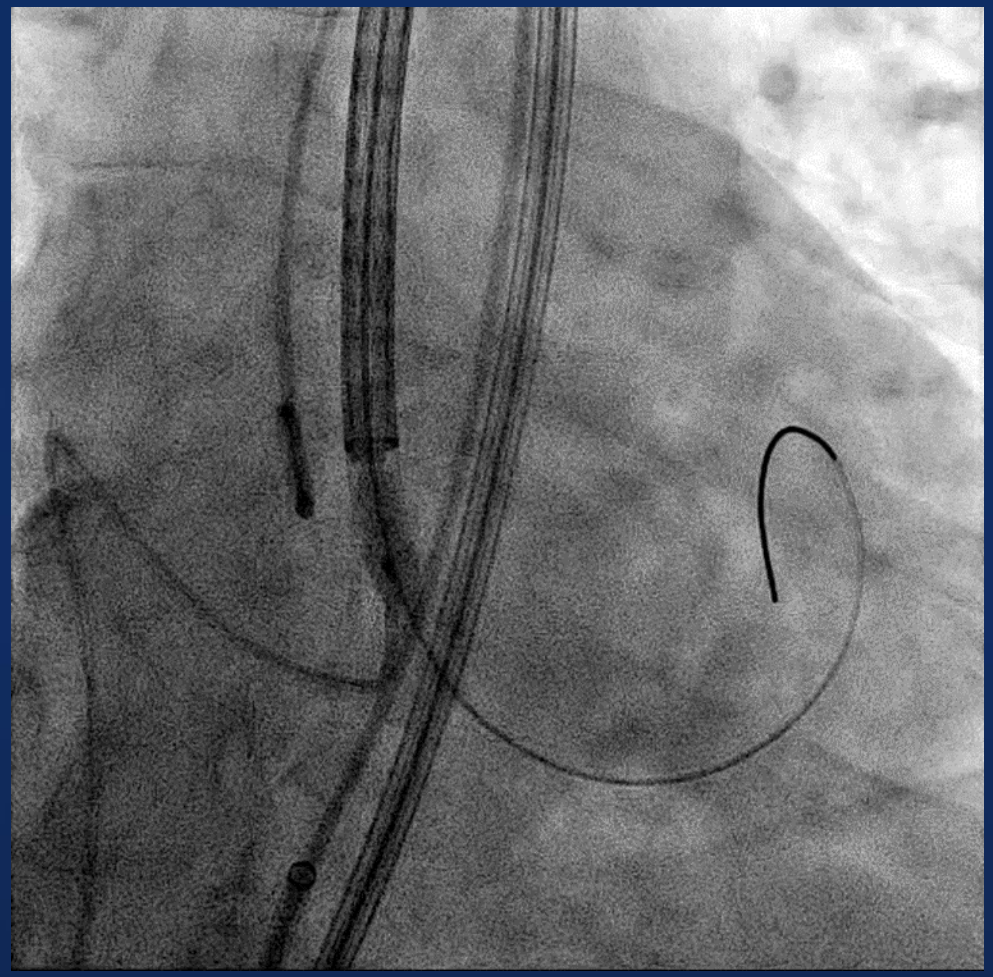
# Starting Position

## 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

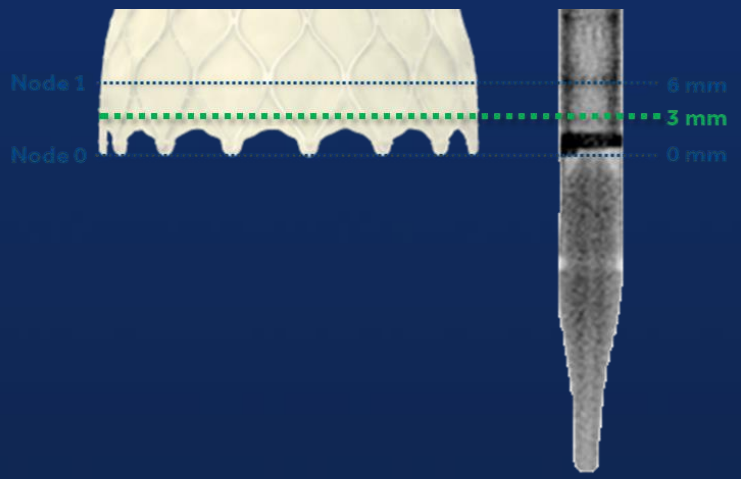


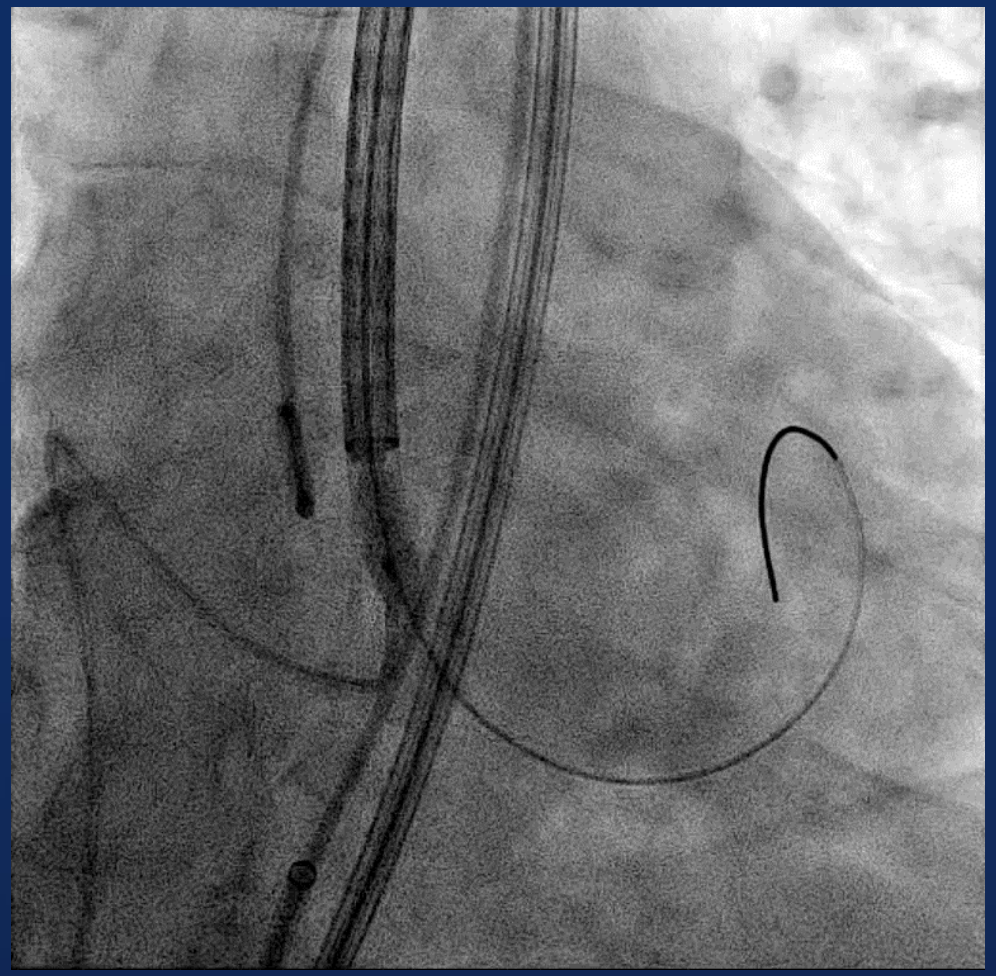
# Initial Deployment

## 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.

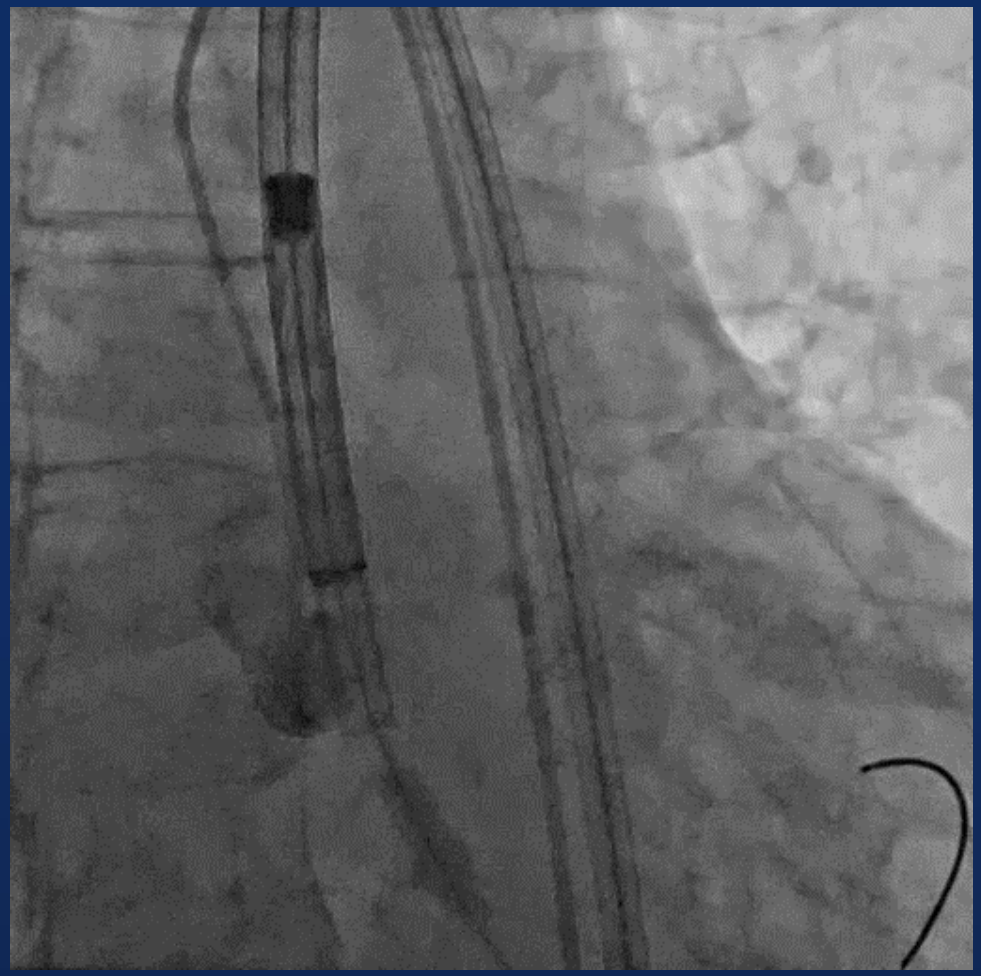
- **Steps**:

- 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.

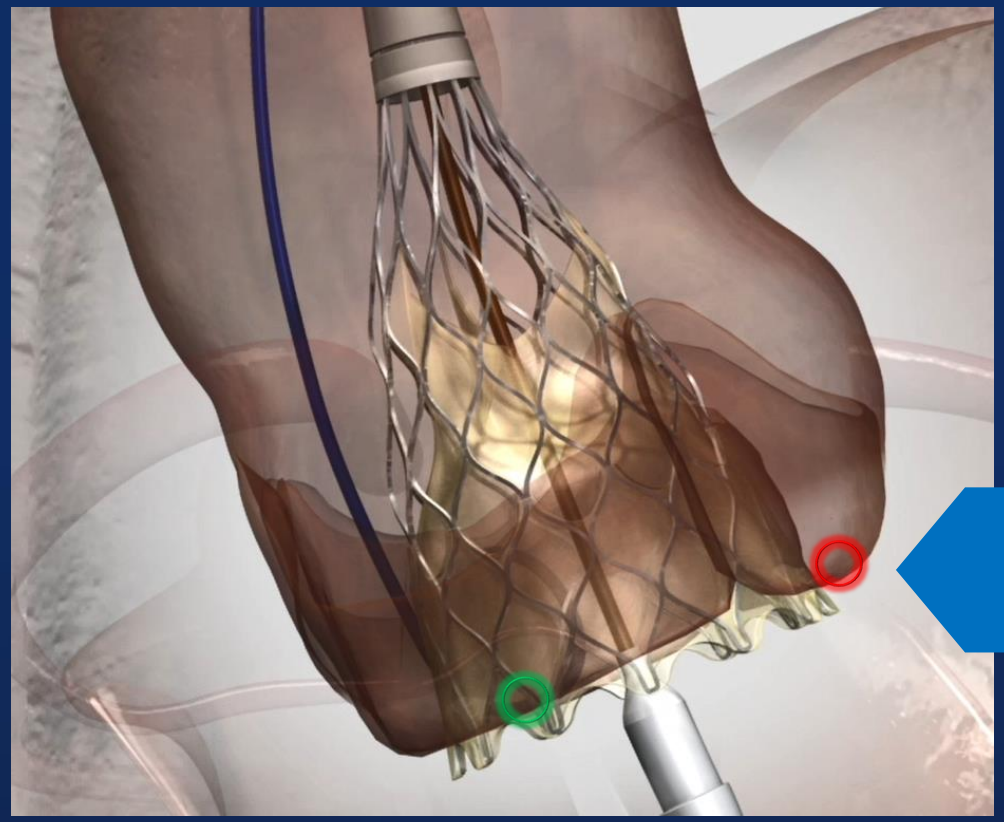
- Rapidly deploy from annular contact to before the point of no recapture as unexpanded bioprosthesis temporarily obstructs cardiac output.

- 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.



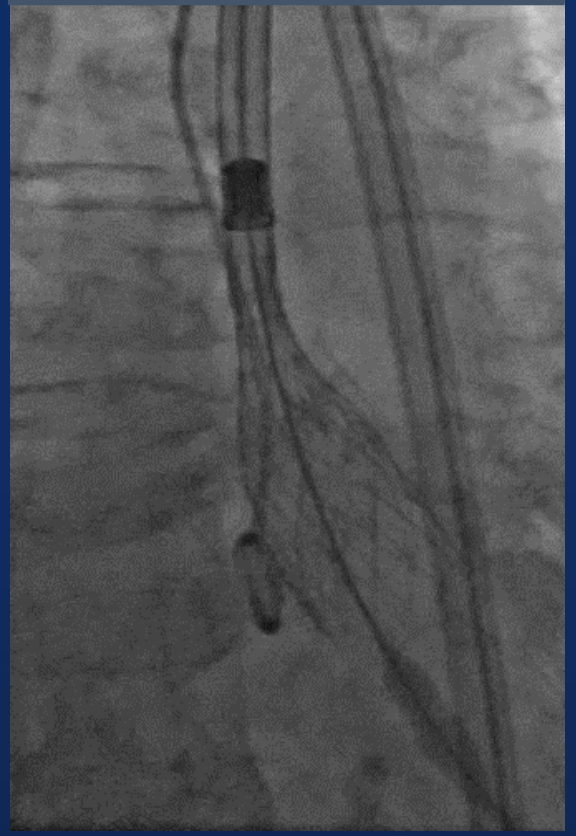
Confirm TAV depth at LCC in the LAO view

# Move to LAO View

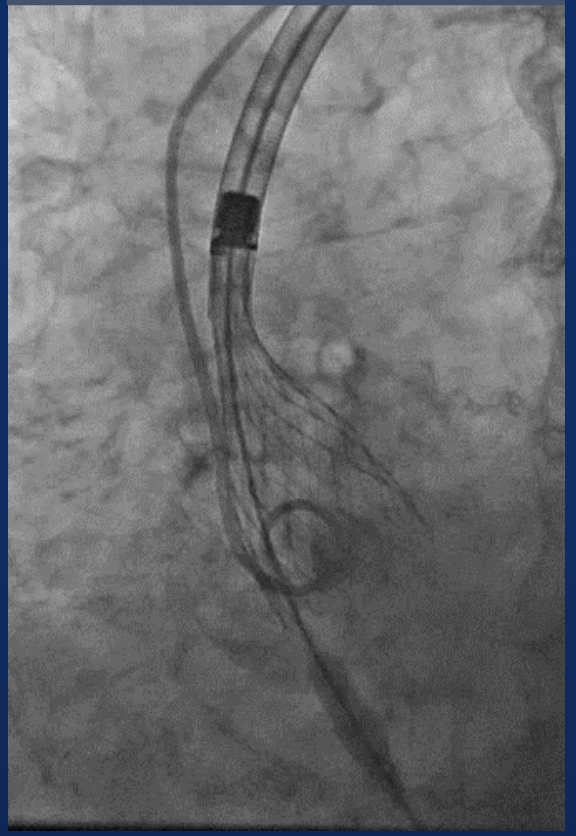
## CONFIRM DEPTH AND PERFORMANCE

- **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



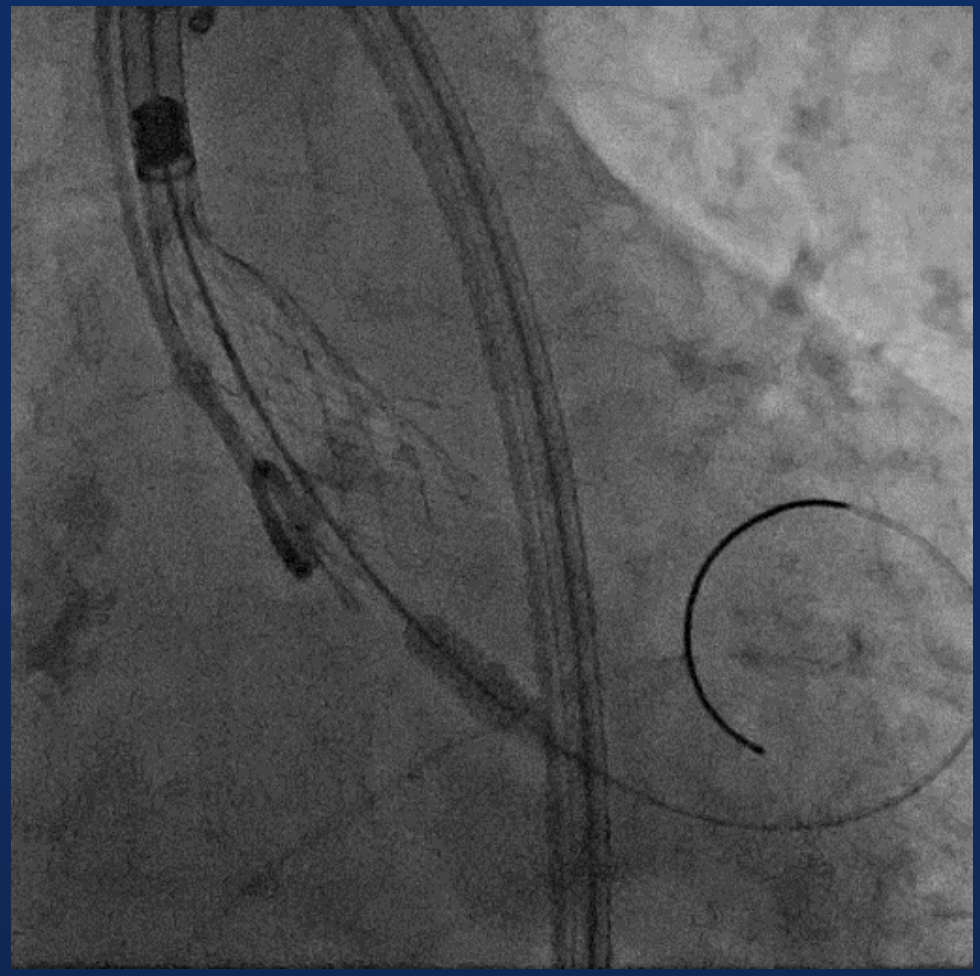
# Recapture Considerations

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.

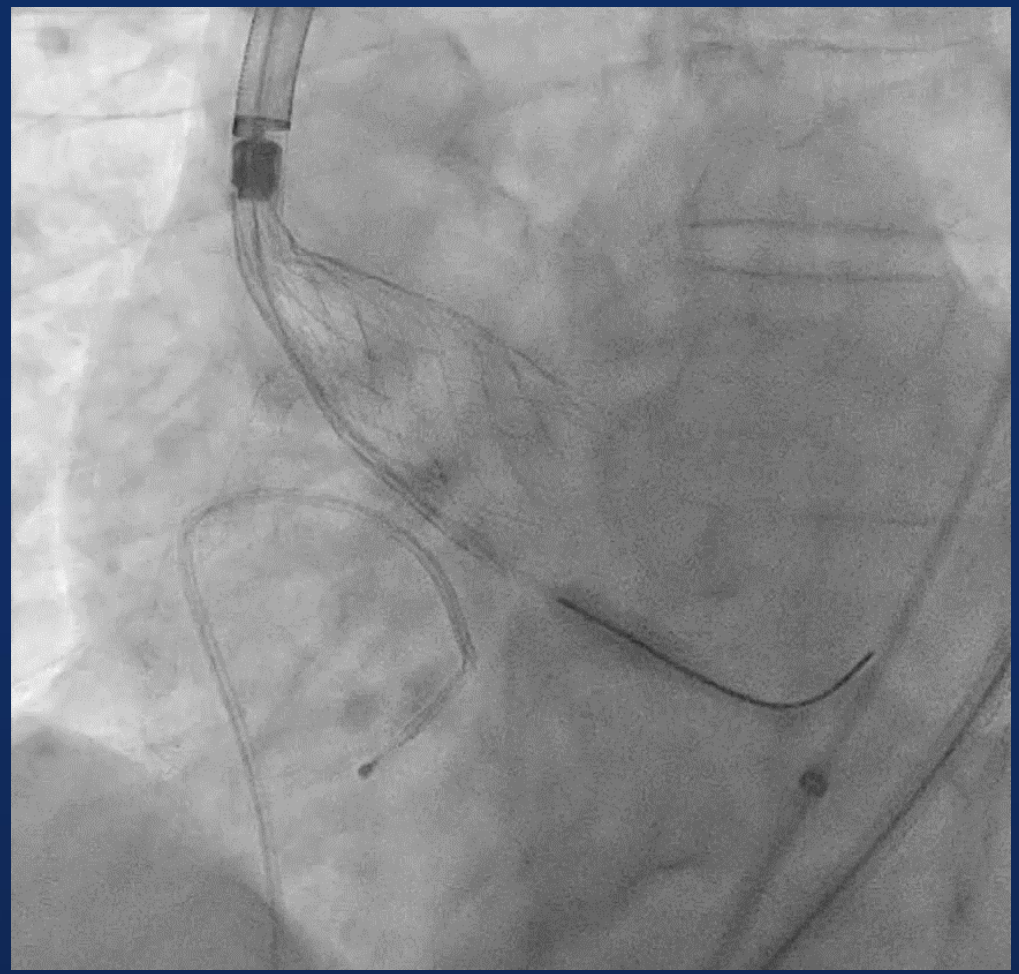
# Deployment

## 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

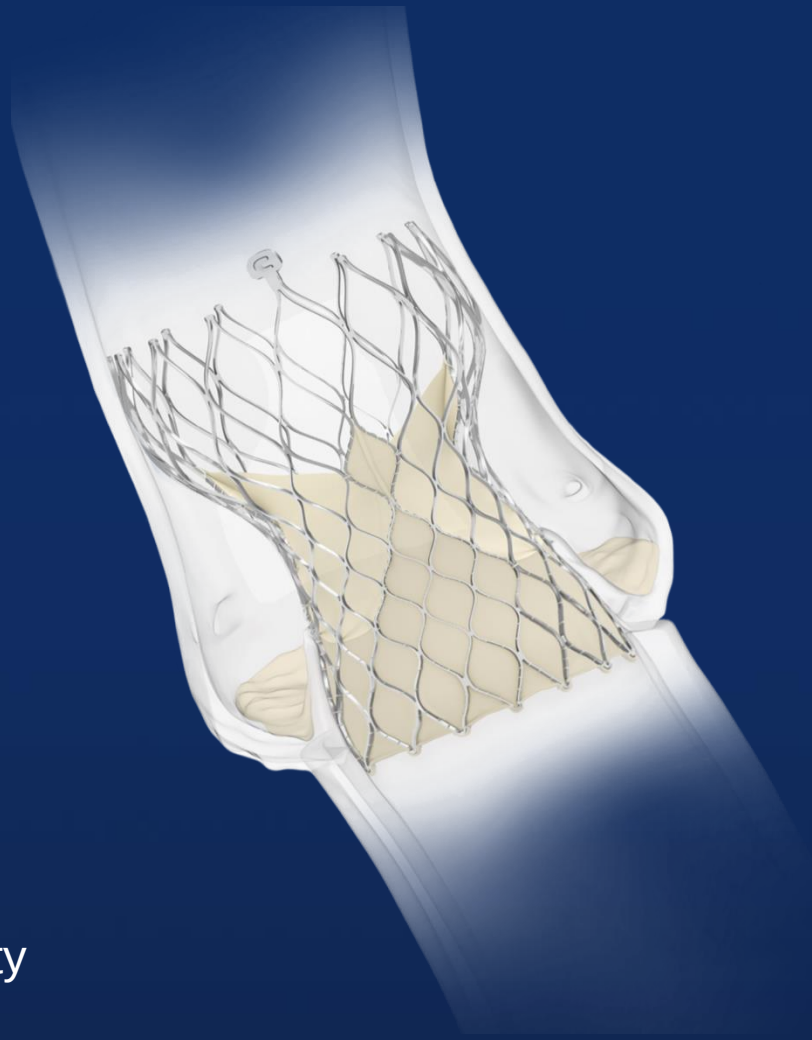
- Conforms and seals to the annulus
- The foundation for recapturability

## Supra Annular Valve Design

- Maximize flow and optimize coaptation

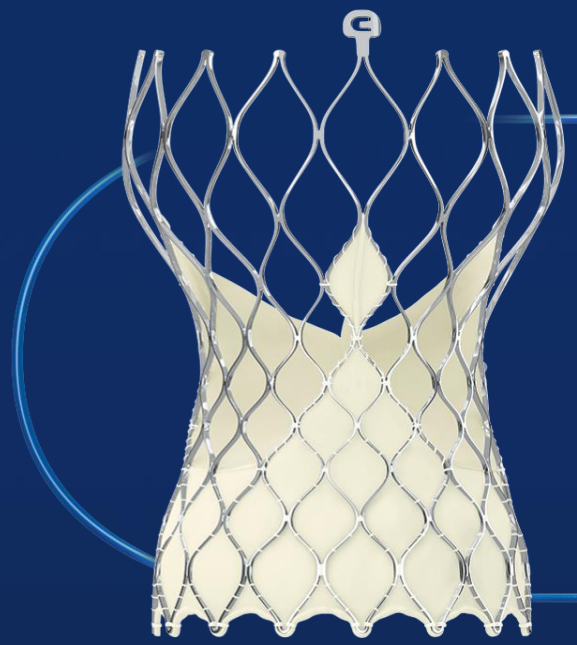
## Porcine Pericardial Tissue

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



# CoreValve Evolut R System

## Recapturable valve and delivery catheter with loading system



Transcatheter Valve

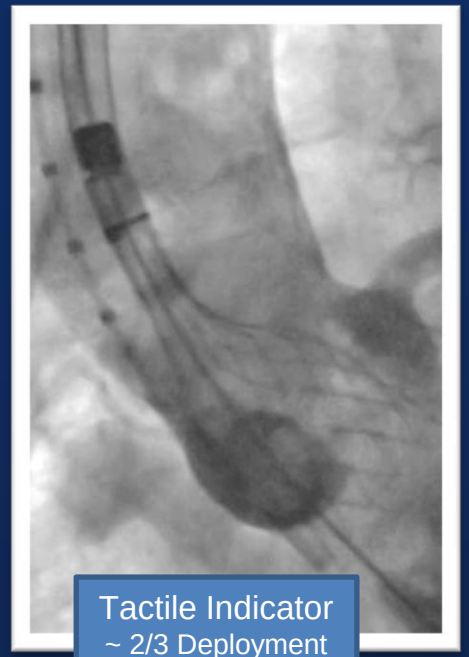

**Catheter Delivery System**

14Fr-equivalent profile

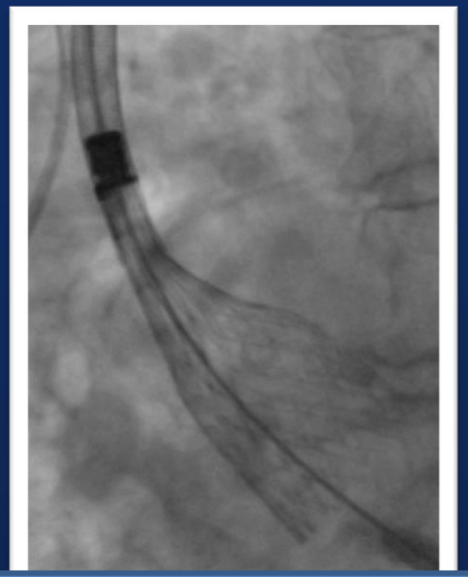
**Loading System**

# 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'*



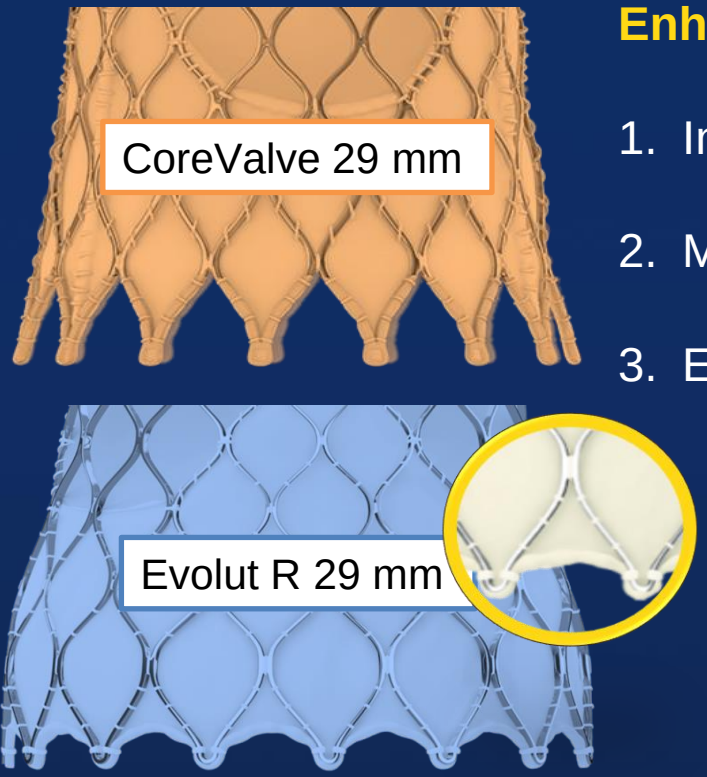
Tactile Indicator
~ 2/3 Deployment



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

* Up to 80% deployment

# Evolut R
# Enhanced Sealing

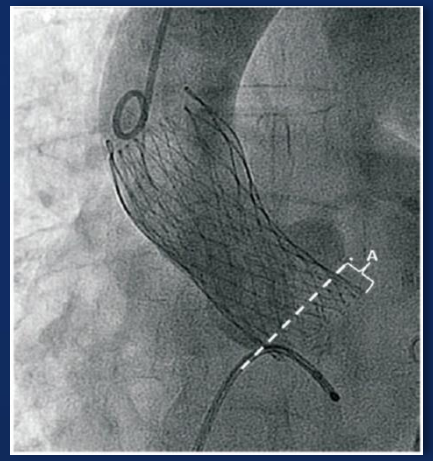



**Enhanced Sealing with a More Conformable Frame ***

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



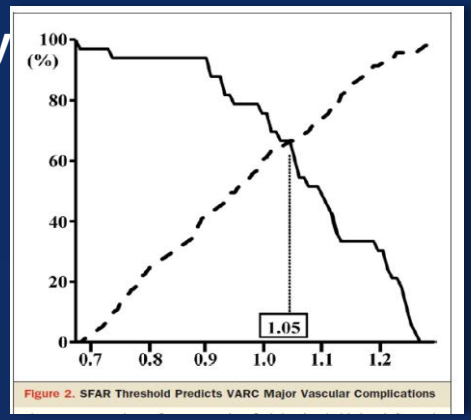
(TcheTche, et. al. – EuroIntervention 2012)

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

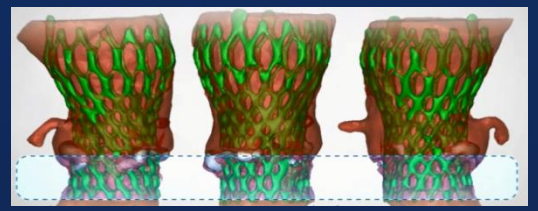
2. **Positioning Accuracy** Key to achieving superior clinical outcomes, including PVL performance and conduction disturbances

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)



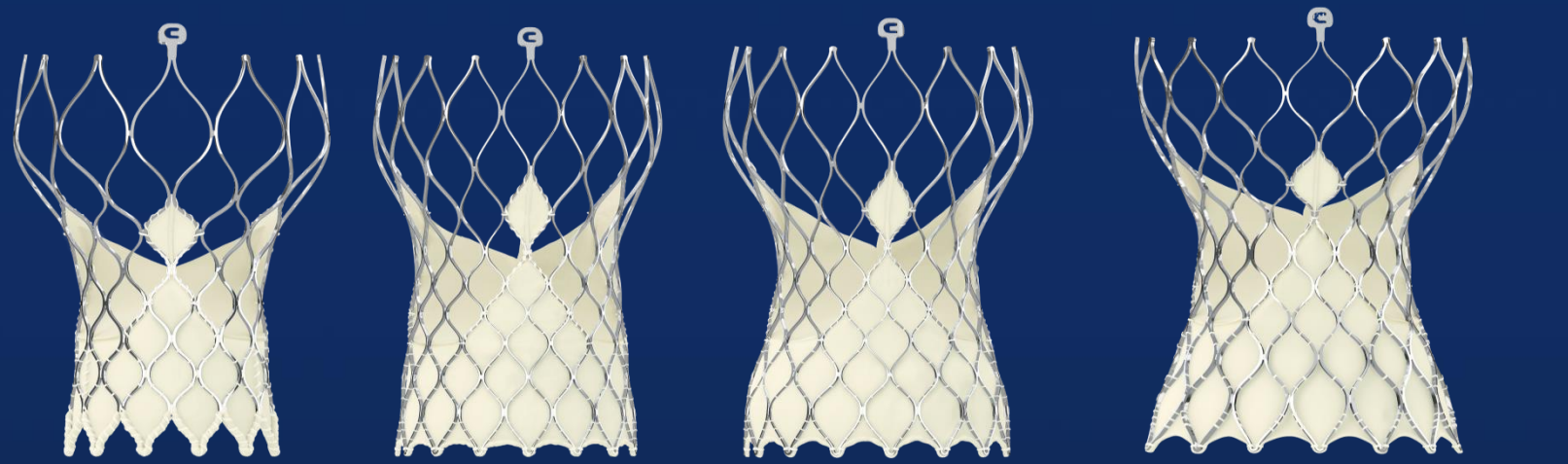
CT images courtesy of Dr. Piazza and Prof. Lange, German Heart Center, Munich Germany

# Evolut R : broad coverage of size

## Indicated Size Range

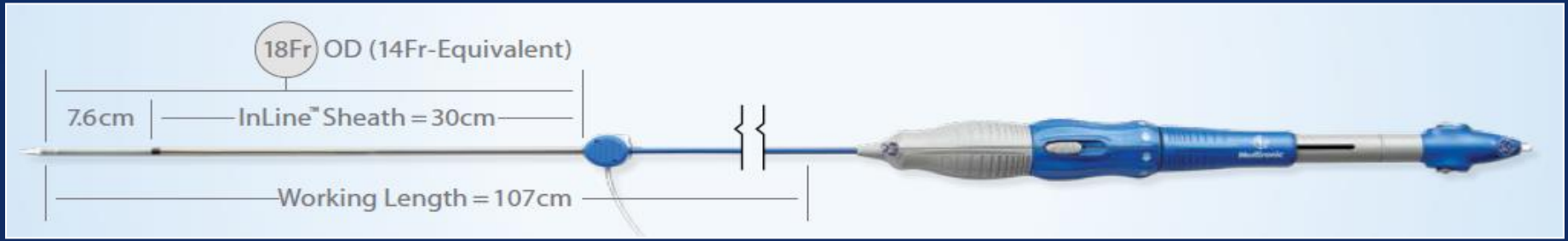
Evolut R 23, 26, 29 mm
CE and FDA Approved

Evolut R 34 mm
Received IDA Approval




Patient Annulus Diameter Range (mm)

# EnVeo R Delivery Catheter Dimensions



# Lowest Delivery Profile

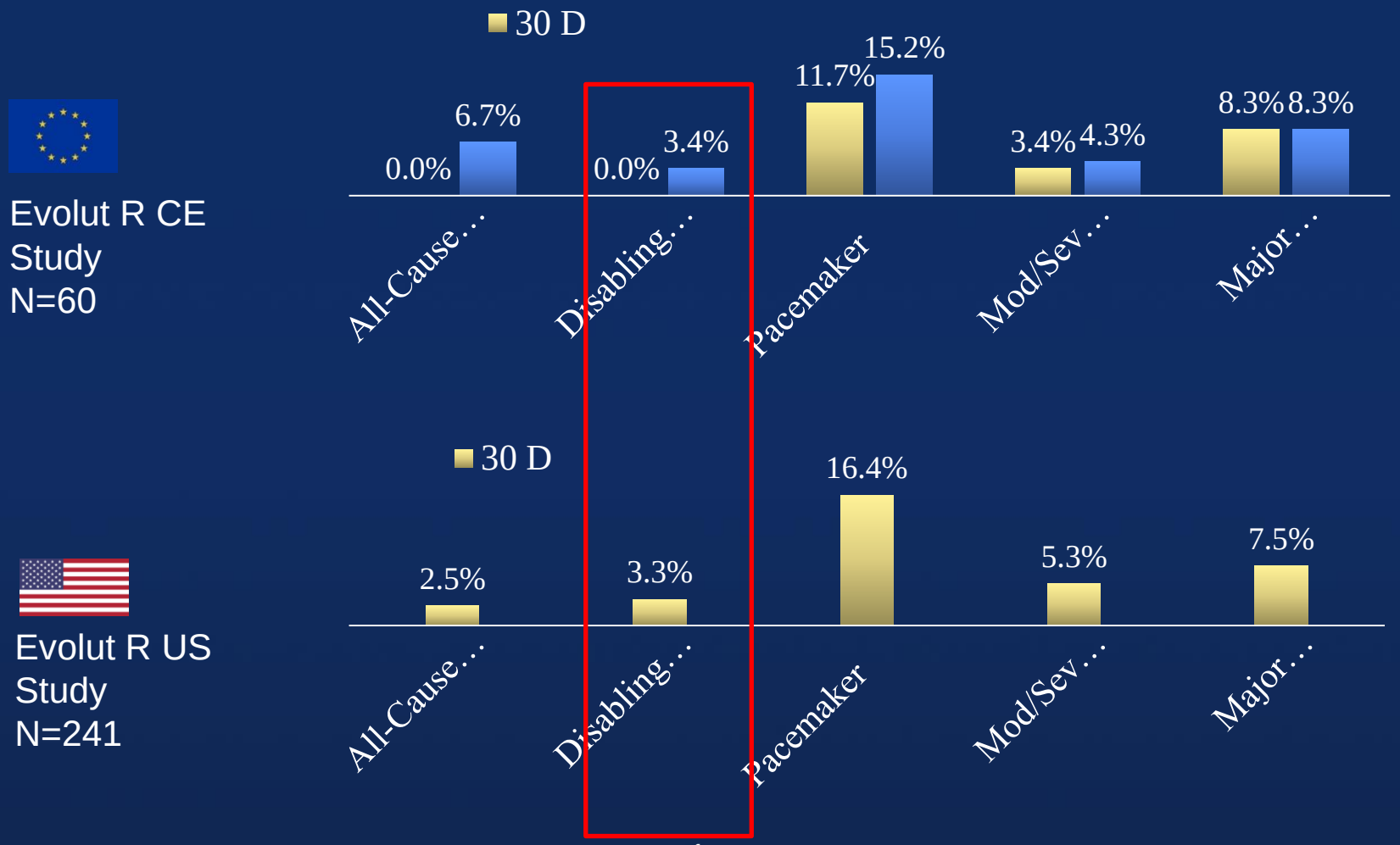
## True 14Fr system with 5mm vessel indication

### Sheath size comparison (Evolut R vs Sapien3)

| Valve Size | 23mm | 26mm | 29mm |
|---|---|---|---|
| **CoreValve Evolut R Device** | | | |
| Minimum Vessel Diameter | 5.0mm | 5.0mm | 5.0mm |
| Outer Diameter | with 14Fr-Equivalent InLine™ Sheath: 18Fr — True 18Fr (OD) | | |
| **Sapien 3 Device** | | | |
| Minimum Vessel Diameter | 5.5mm* | 5.5mm* | 6.0mm* |
| Inner Diameter / Outer Diameter / Expanded Outer Diameter | 17.4Fr△ (14Fr) / 23Fr† | 17.4Fr△ (14Fr) / 23Fr† | 19.5Fr△ (16Fr) / 24.5Fr† |

# 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

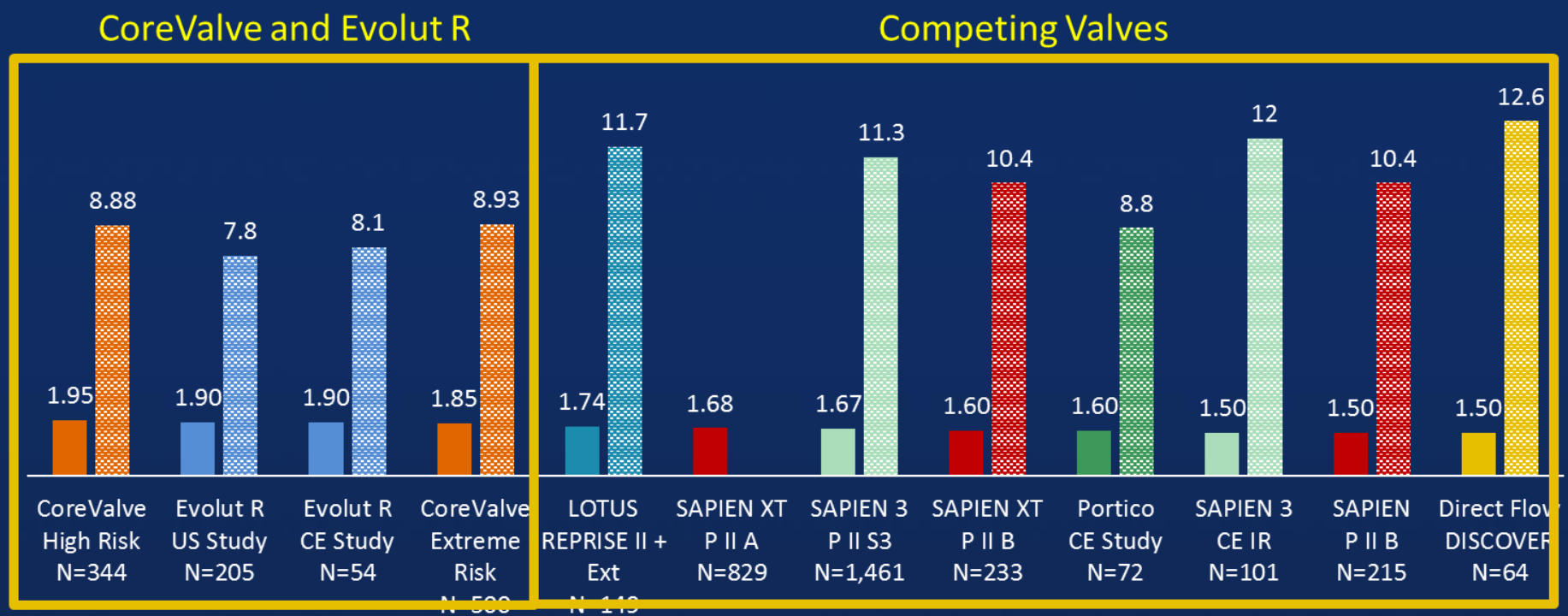
Evolut R

Sapien 3

Lotus

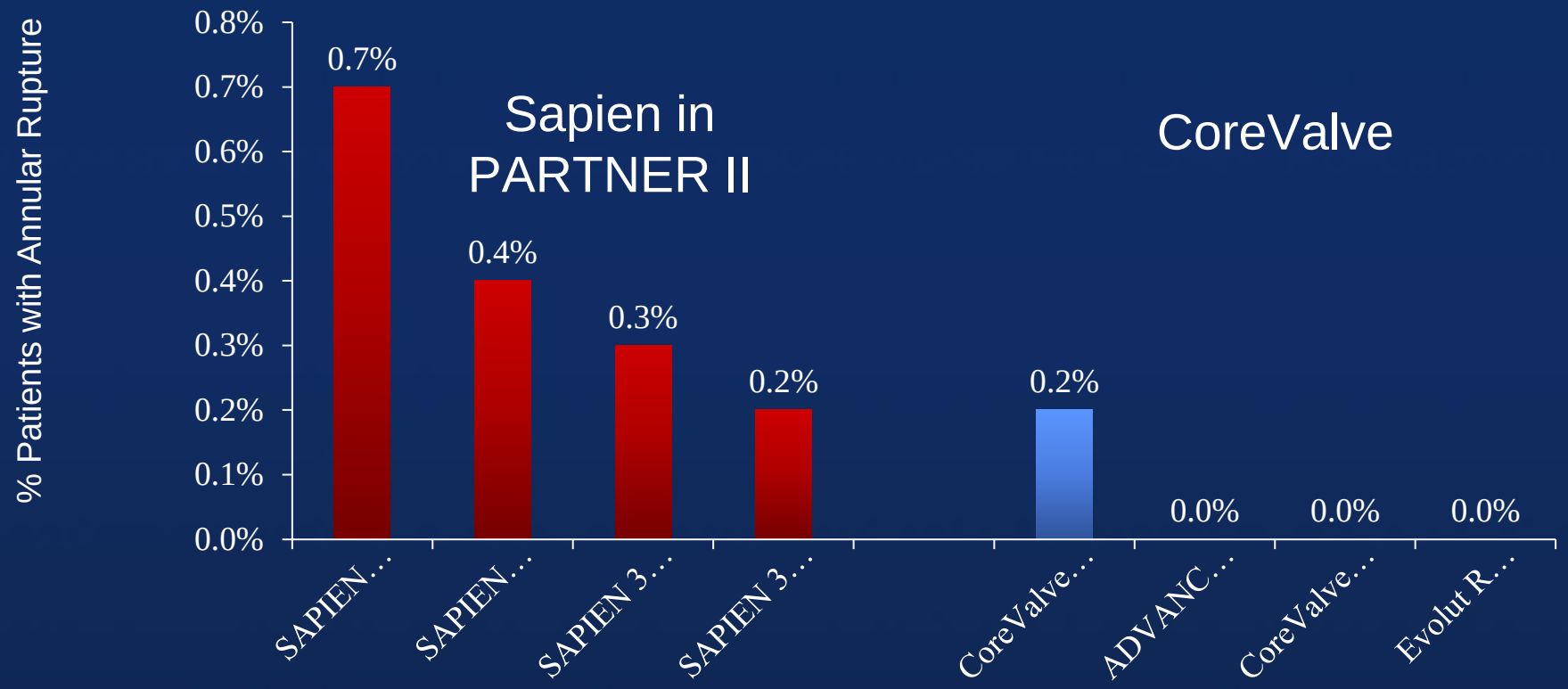
# Hemodynamics : best d/t wide orifice area

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



# Evolut R : Annular Rupture is Rare

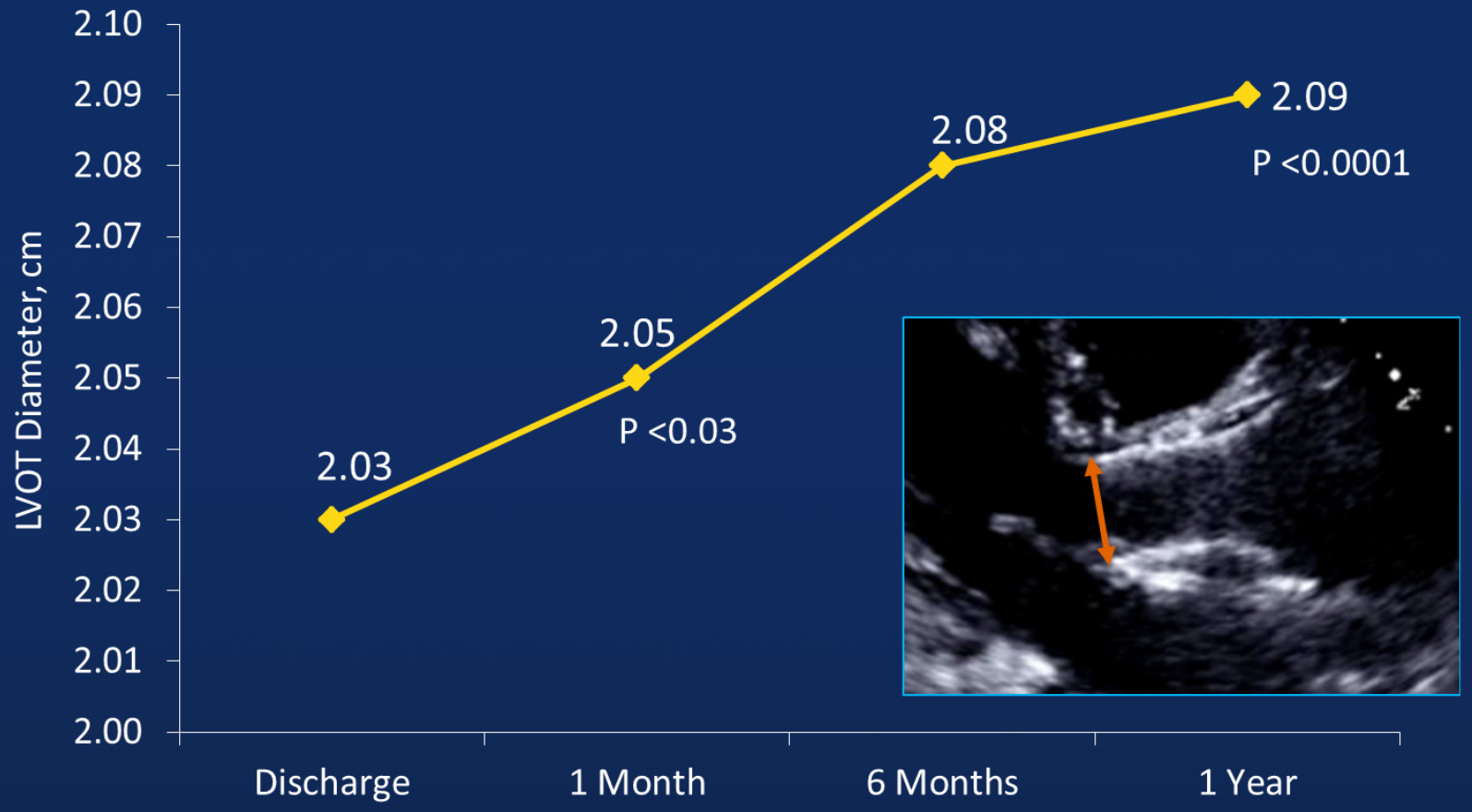
Annular rupture is mainly associated with the inflation of a balloon,
either during valve deployment or pre- or post-dilation



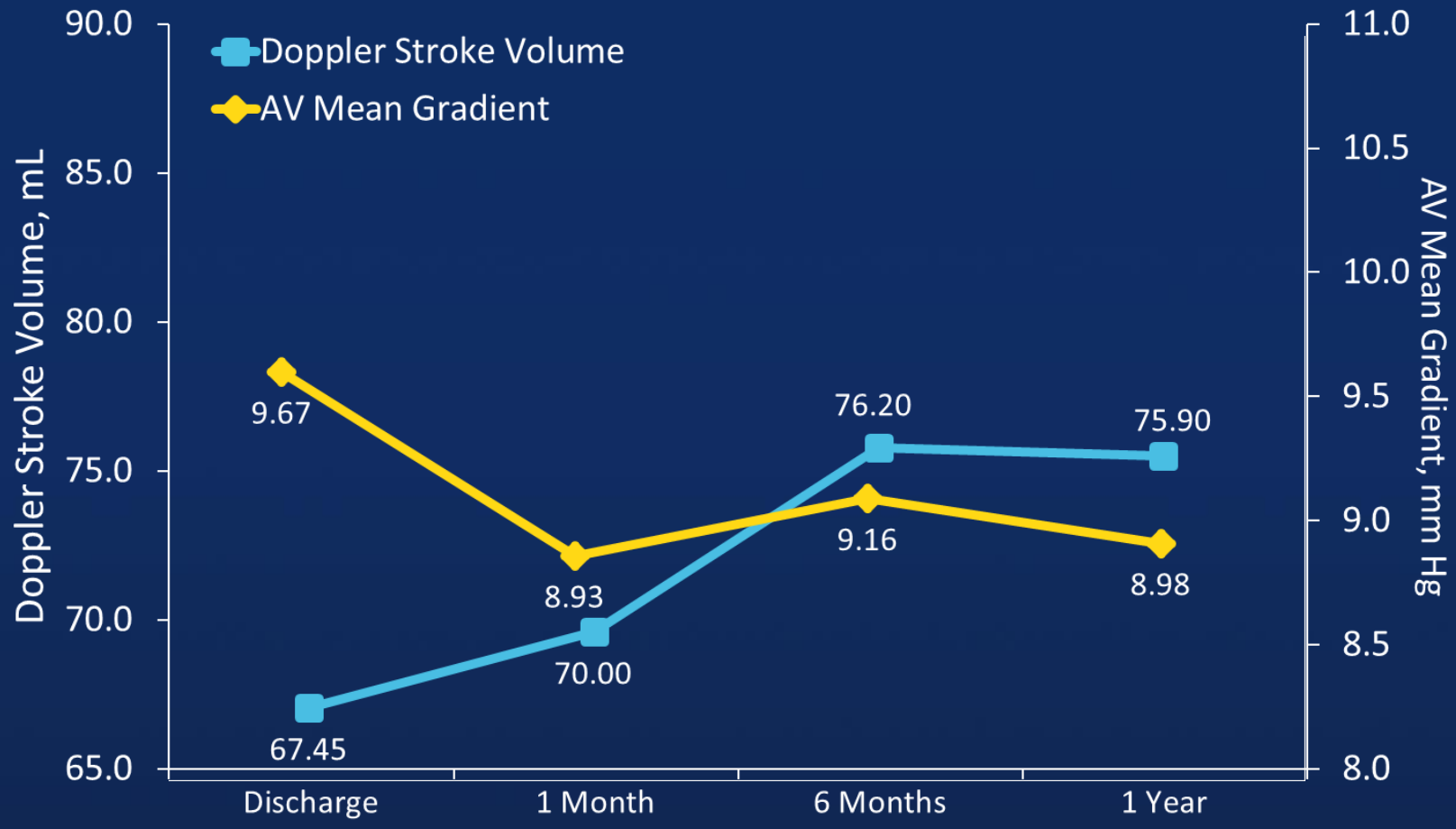

[1]Leon, et. al. presented at ACC 2013; [2]Kodali, et al., presented at ACC 2015; [3]Popma, et al., J Am Coll Cardiol 2014; 63: 1972-81;
[4]Linke, et al. , Eur Heart J 2014; 35: 2672-84; [5]Adams, et al., N Engl J Med 2014; 370: 1790-8; [6]Meredith, et. al. presented at EuroPCR 2015

# Evidence of Continued Outward Expansion

## LVOT Diameter Outer to Outer Edge

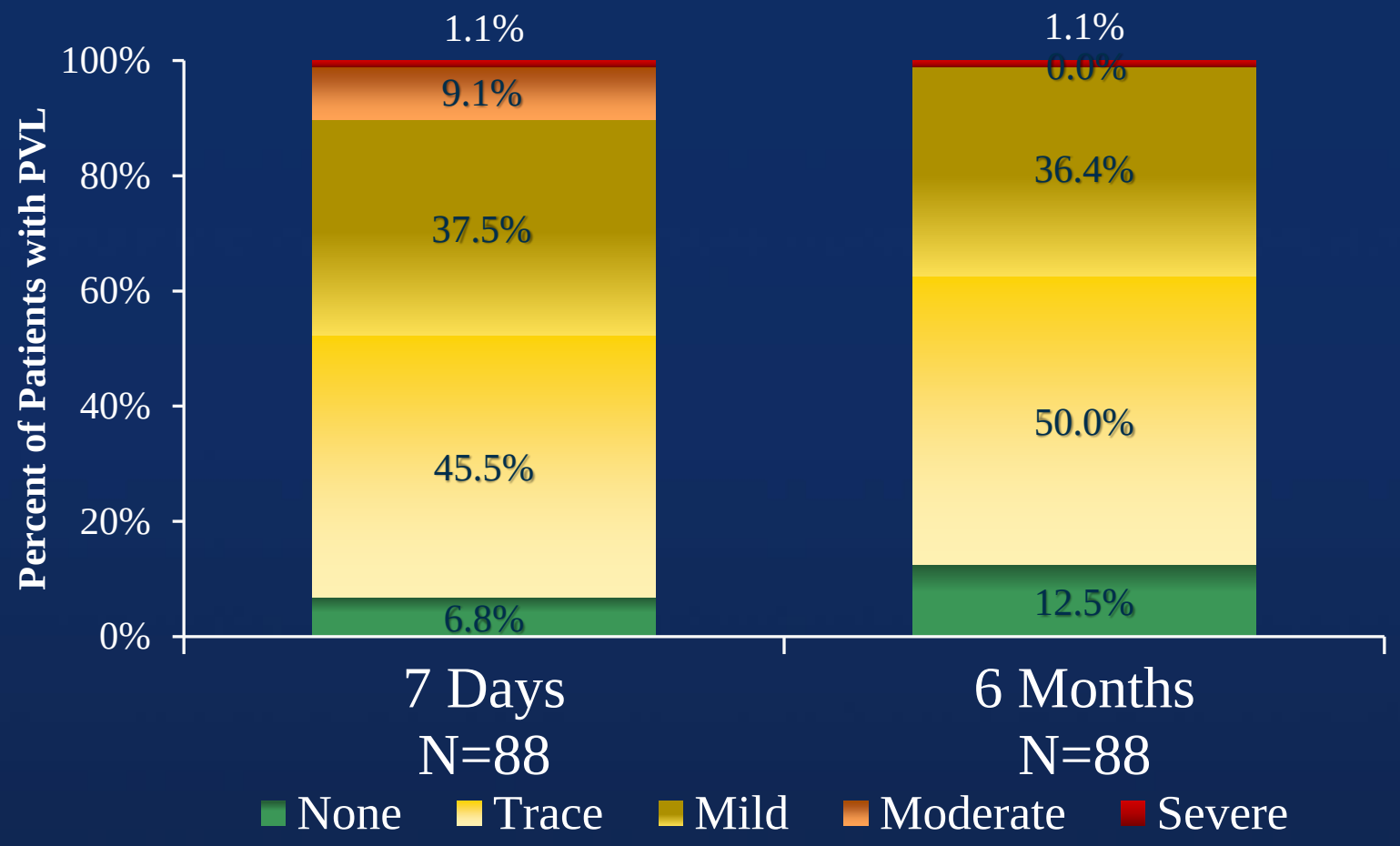


# Continued Outward Expansion
## Leads to Reduction in AV Gradient



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

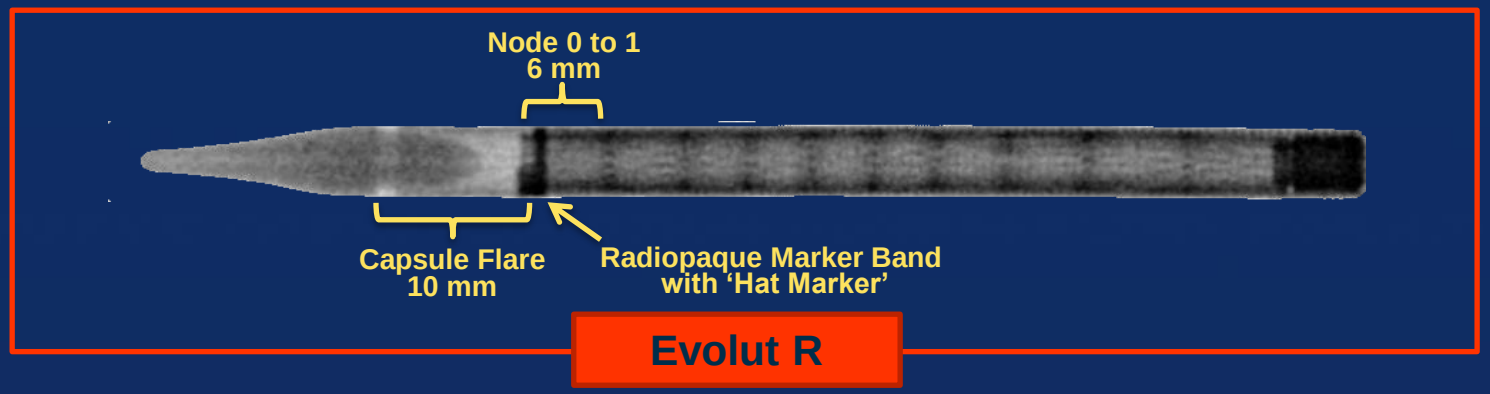
Paired data show >mild PVL decreased significantly from day 7 to 6 months (p=0.005†)

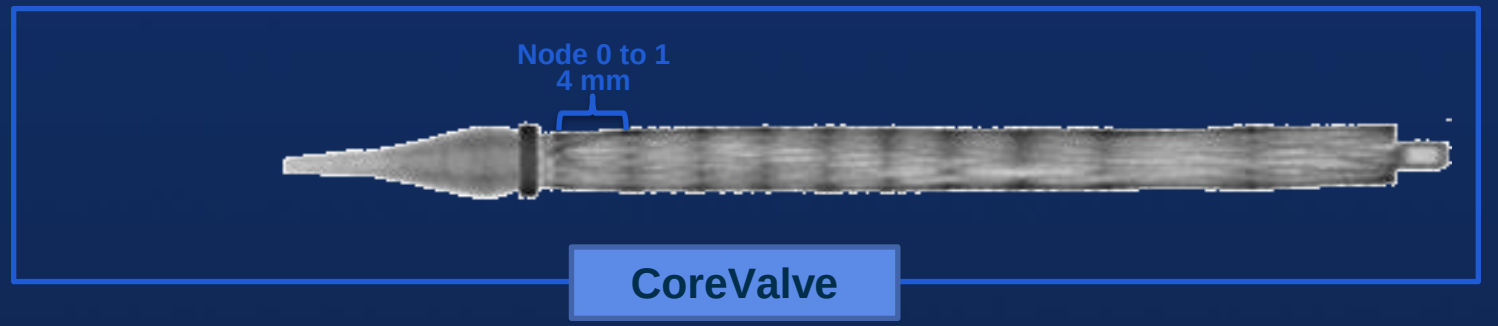



†McNemar's test on paired data

*CoreValve ADVANCE II Study*

# Loaded Capsule under Fluoroscopy



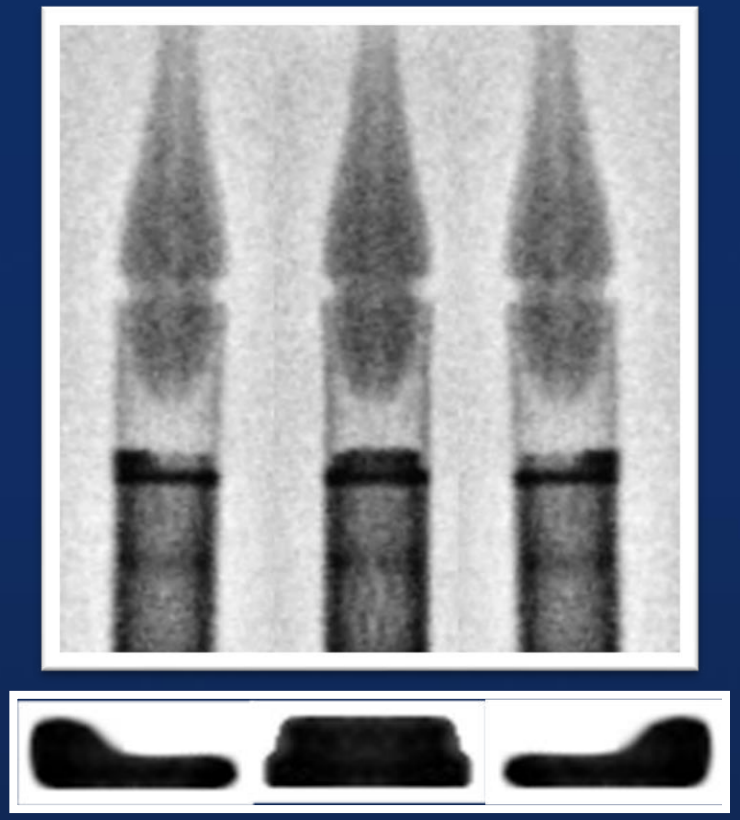




Note: Measurements provided are approximate based on engineering specifications.

# 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

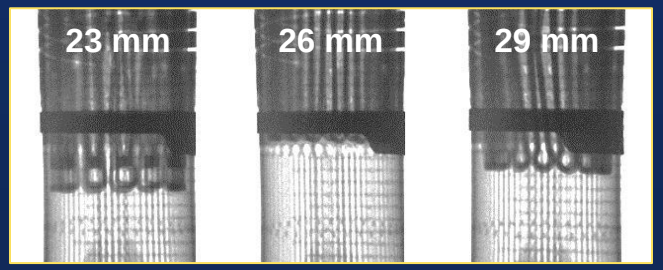
- Resembles a hat when viewed under fluoroscopy
- Used to assess delivery system orientation

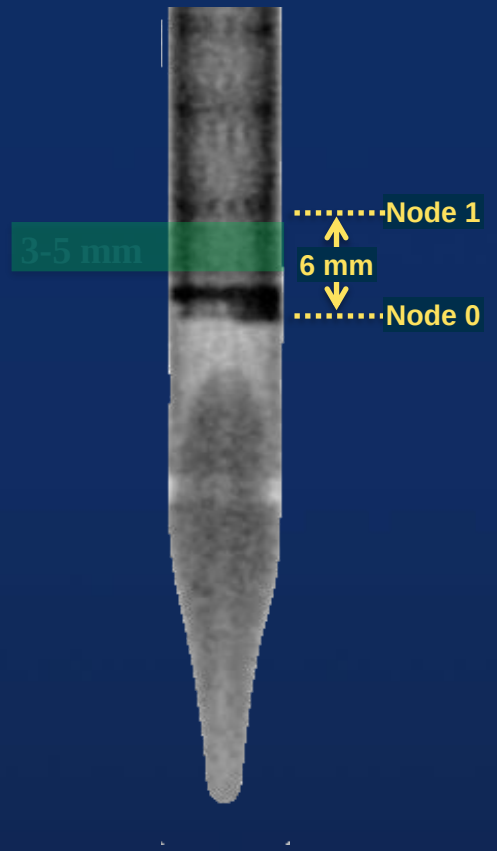


# Evolut R Target Implant Depth

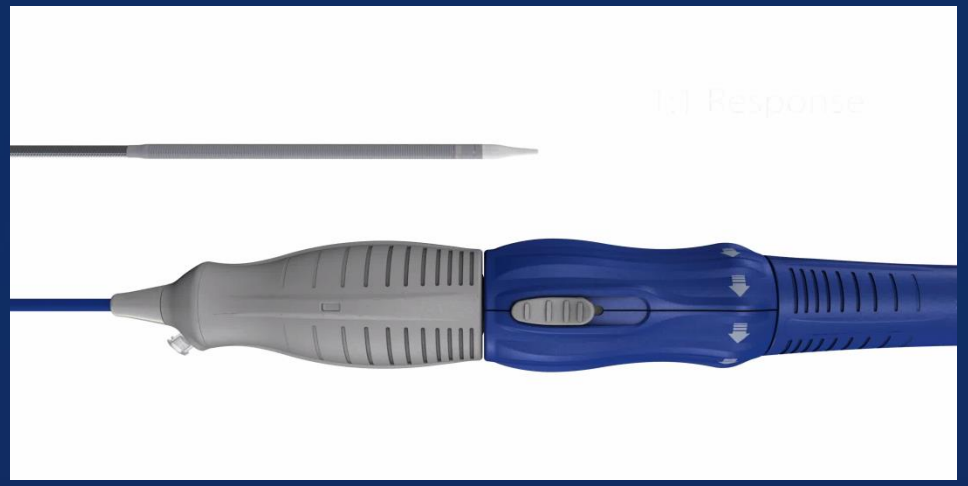
Target implant depth is **3 - 5 mm**

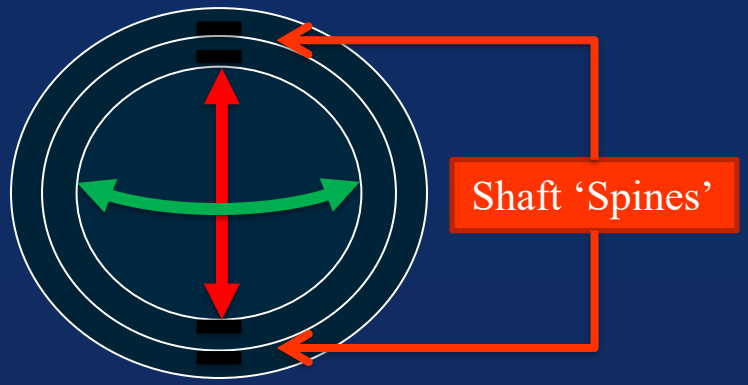
- Midway between node 0 (inflow edge of frame) and node 1 to just below node 1
- Note: due to minor valve frame length differenc es, ensure to assess valve position from frame inflow (node 0) and not the edge of the marker band:



# Positioning Accuracy: 1:1 Response



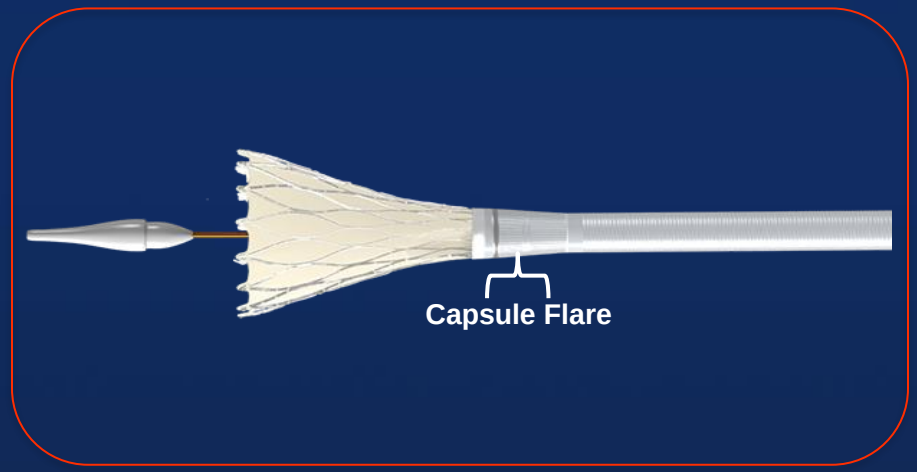



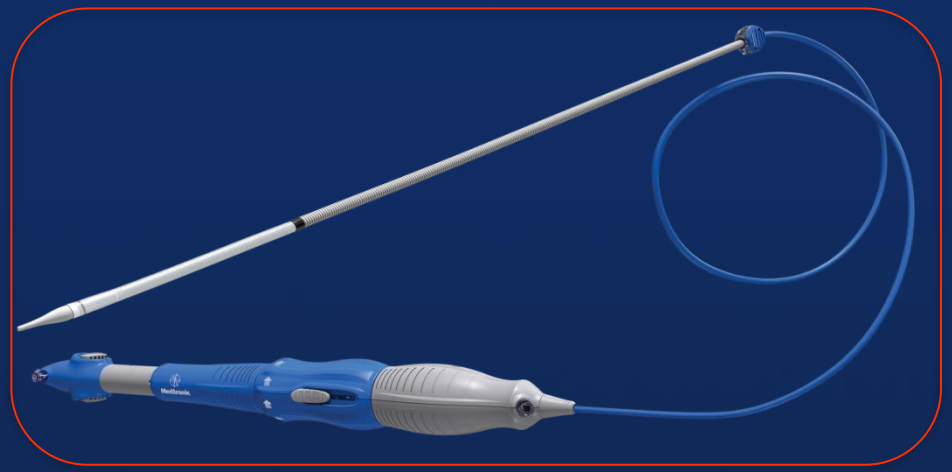

Cross section of catheter shaft
(excluding the stability layer)

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

# Positioning Accuracy: Self-Centering

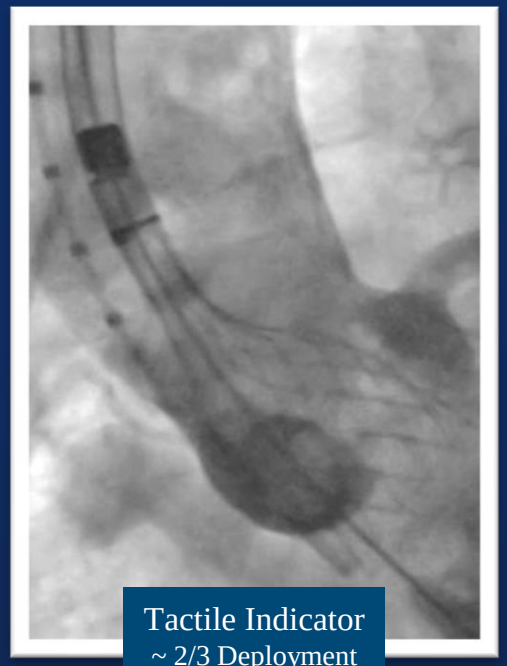
**EnVeo R's Capsule flare and flexible catheter design enable uniform and controlled valve expansion and self-centering of the valve in the annulus**



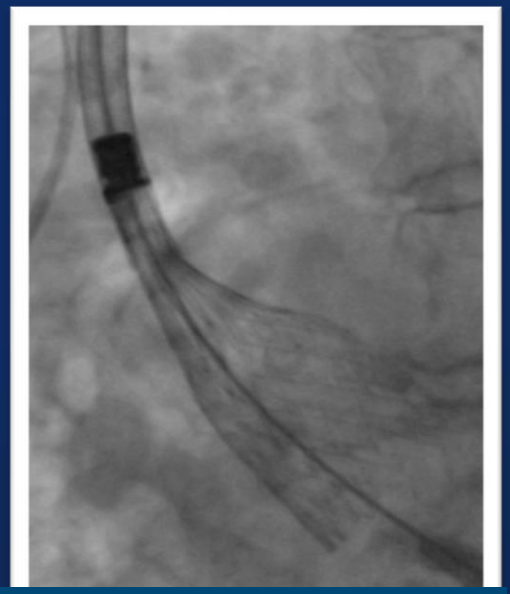



# Positioning Accuracy: Ability to Recapture and Reposition

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



Tactile Indicator
~ 2/3 Deployment

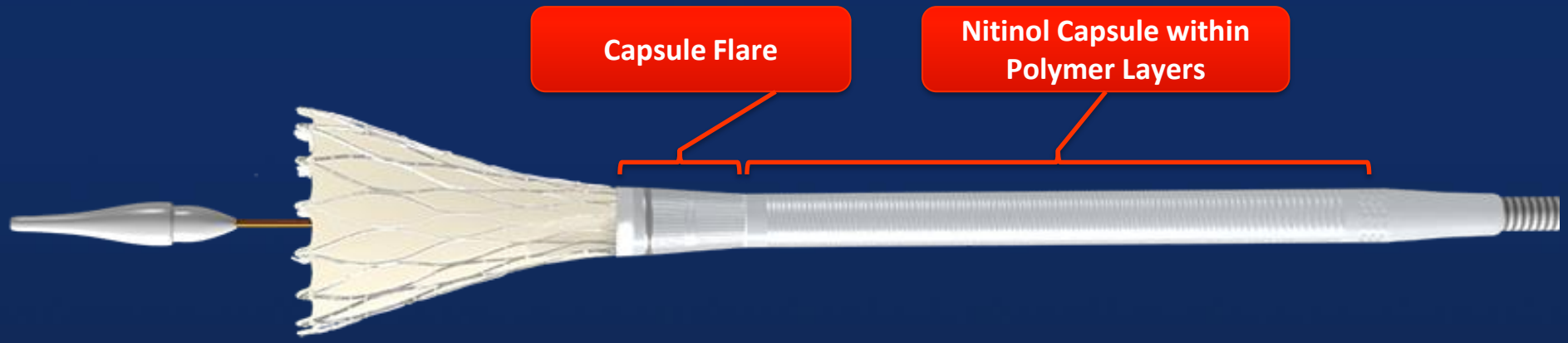


Just Prior to Point of No Recapture
~ 80% Deployment*

* 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.**

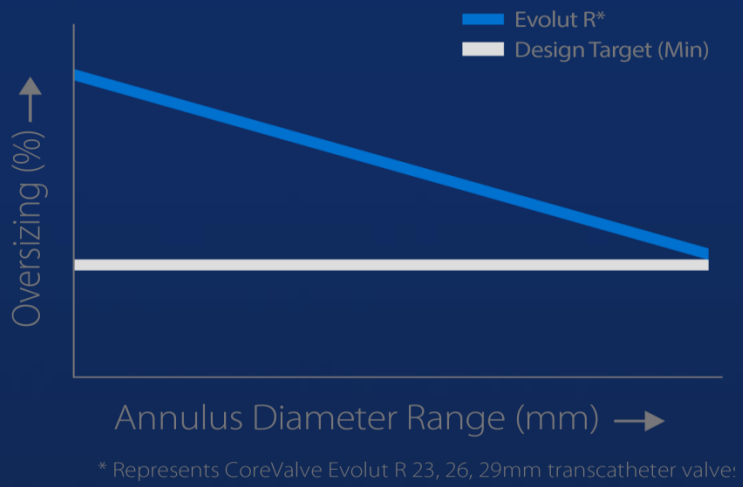


# Enhanced Sealing: Optimized Oversizing, Consistent Radial Force, and Extended Sealing Skirt[1]

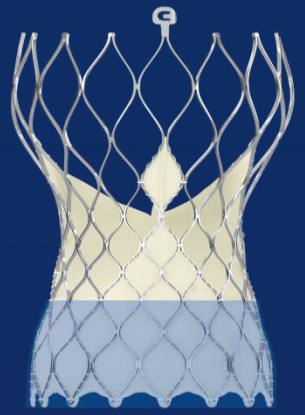
***For Exceptional Valve Performance and Reduced Significant PVL[2]***

## Optimized Oversizing

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

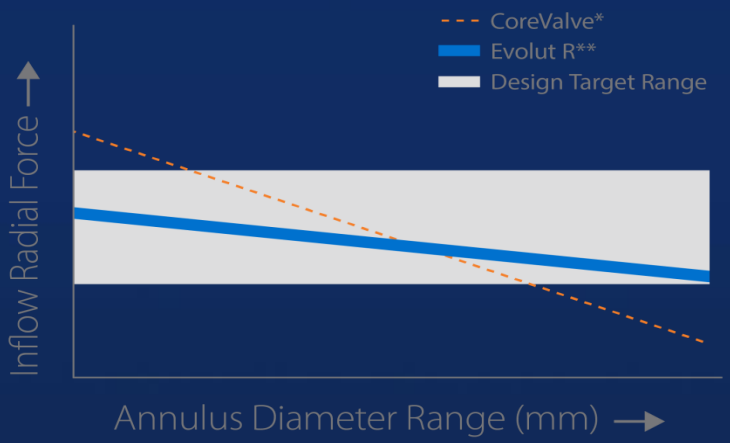



* Represents CoreValve Evolut R 23, 26, 29mm transcatheter valves



## Consistent radial force

Contributes to improved sealing across indicated annulus range for each valve




* Based on combined radial force curve for CoreValve 26, 29 and 31 mm transcatheter valves.

** Based on combined radial force curve for CoreValve Evolut R 23, 26, 29mm transcatheter valves

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

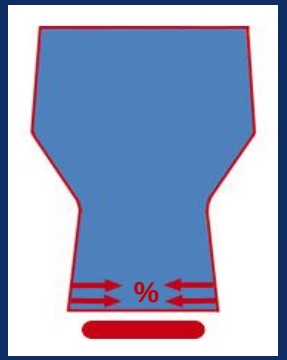
## Oversizing

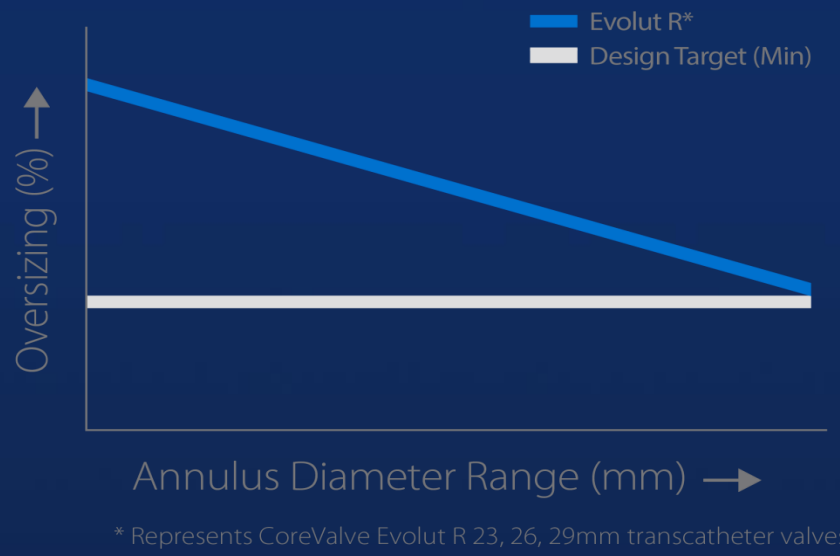
- The size of the bioprosthesis inflow dia meter relative to the native annulus:

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

## Evolut R Design

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



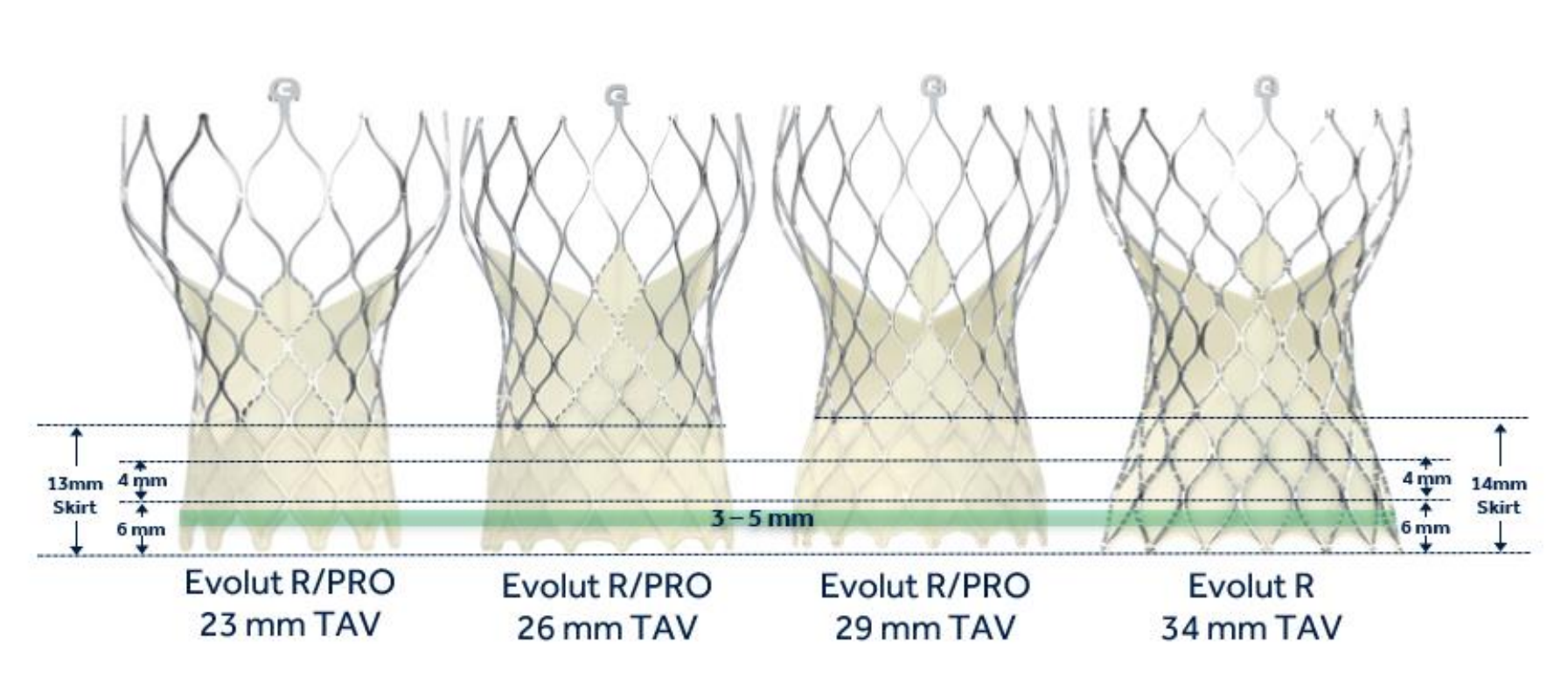




* Represents CoreValve Evolut R 23, 26, 29mm transcatheter valves

# Evolut TAVR Platform

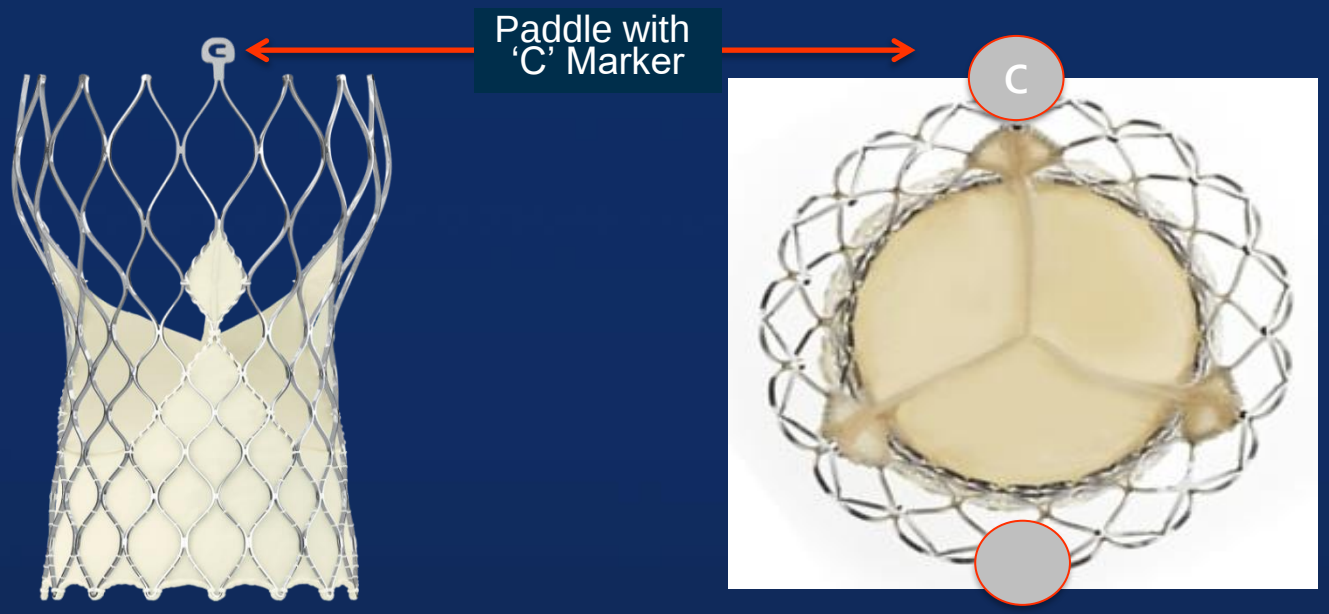
## CELL DIMENSIONS & SKIRT HEIGHT

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

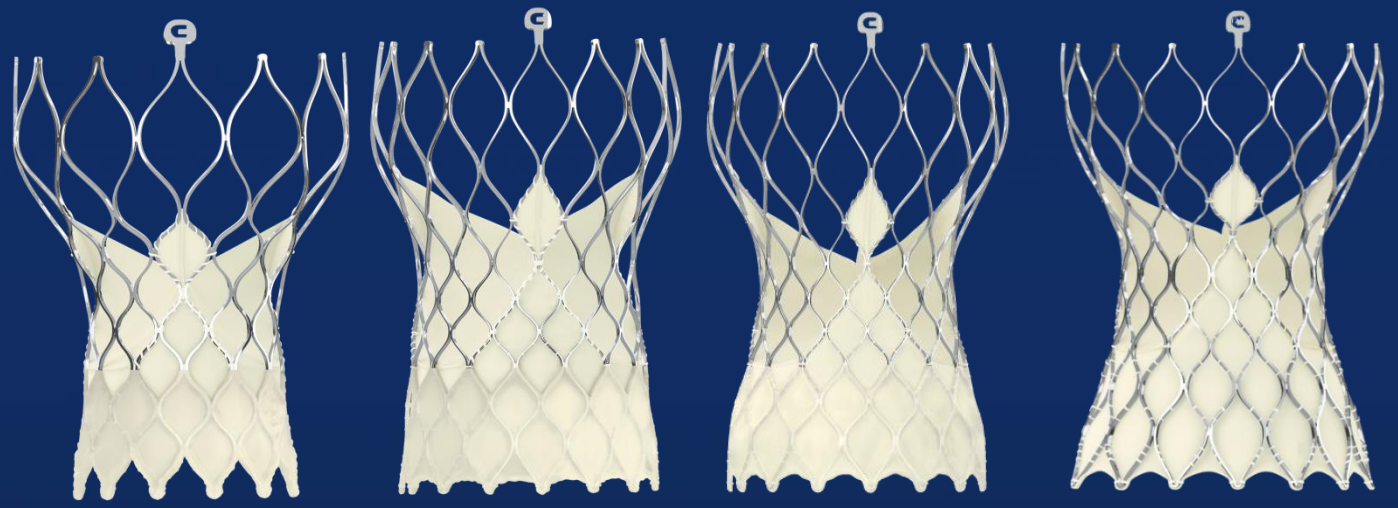



‘C’ marker on one paddle aligns with commissure to help assess post deployment commissure orientation.

# 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***




| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 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**

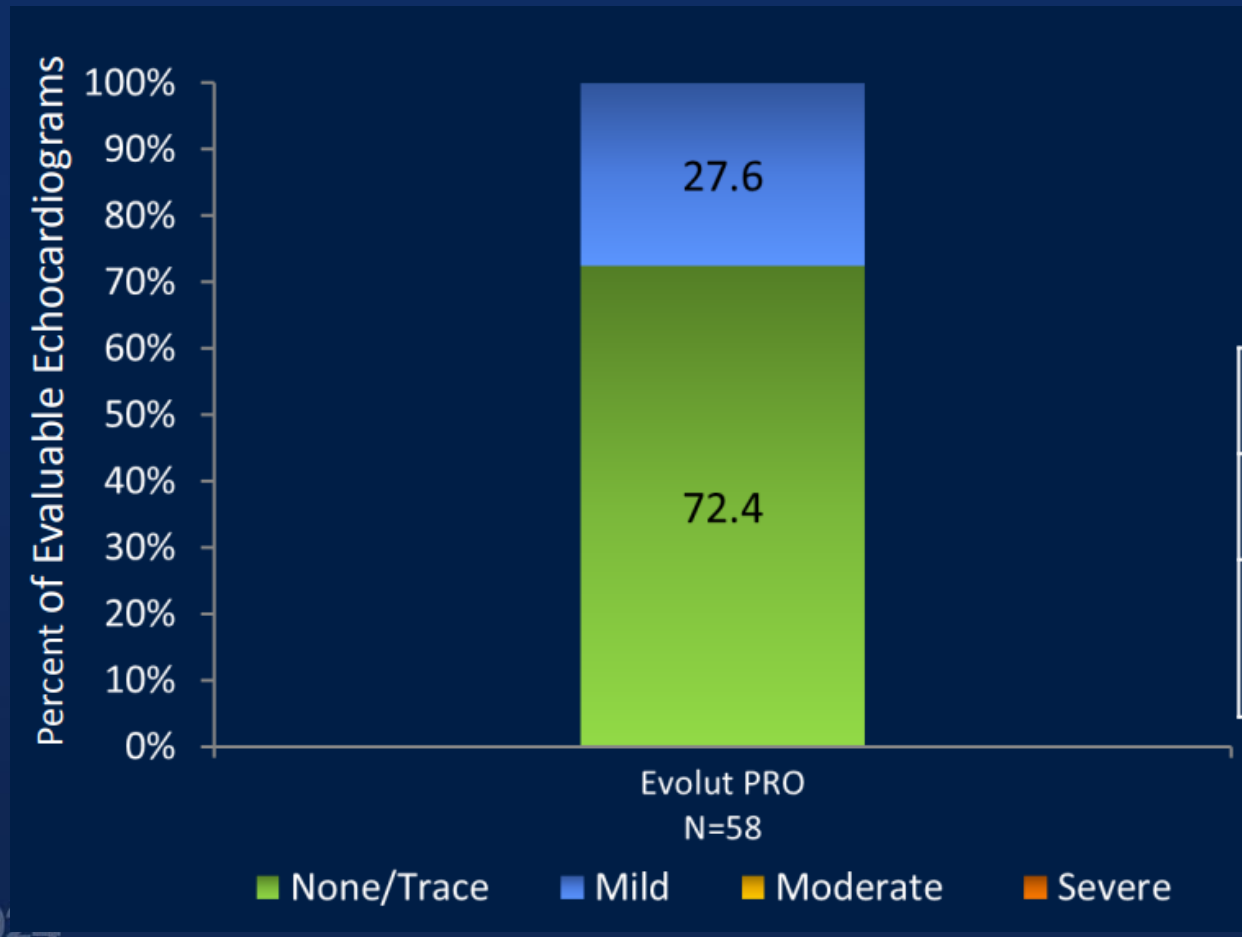
- Conforming frame and consistent radial force provide contact at multiple levels in various annulus shapes
- External tissue wrap increases surface contact area

**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%** |



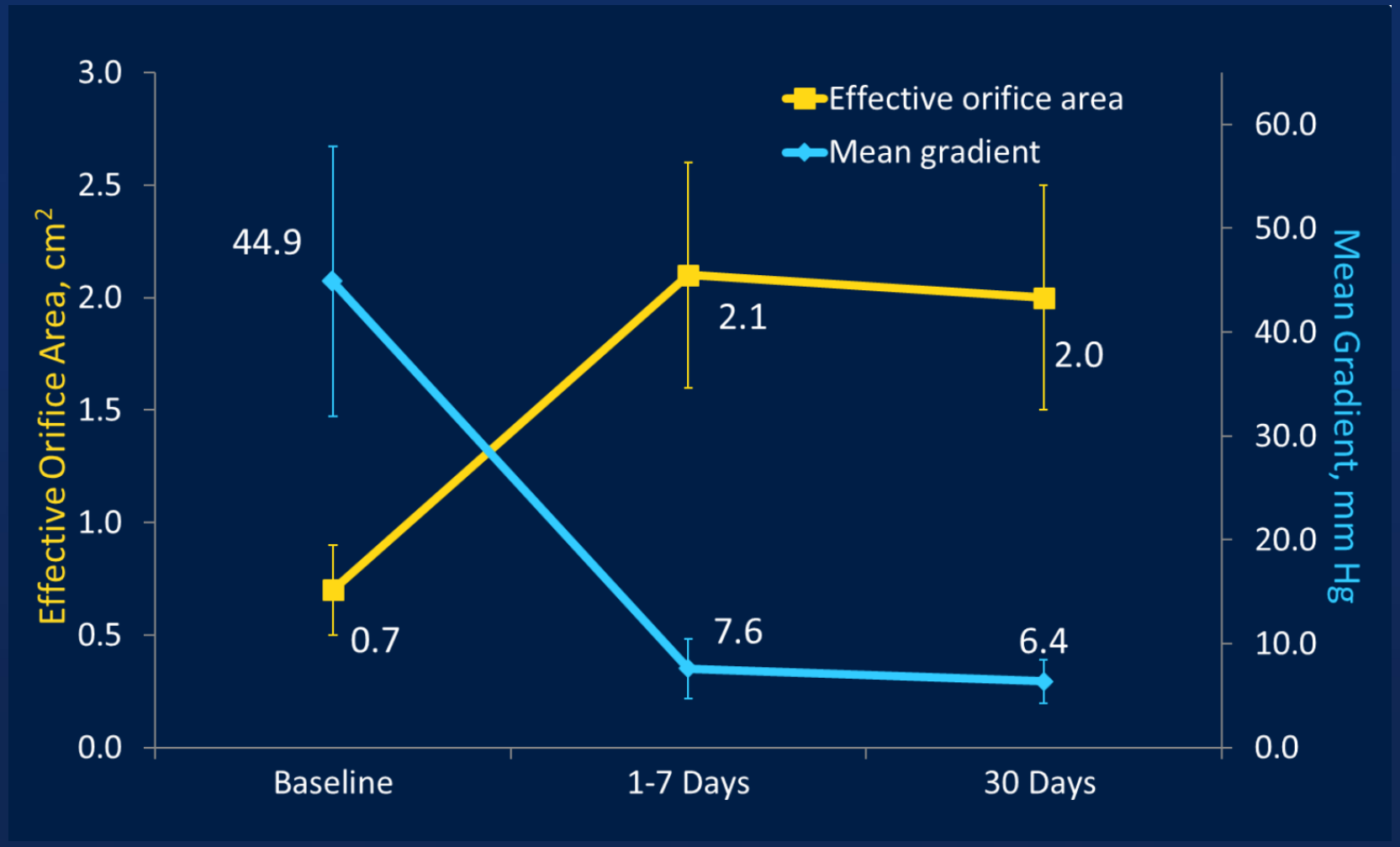
Medtronic

CVRF

Forrest, et al. ACC, 2017

# Evolut PRO

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





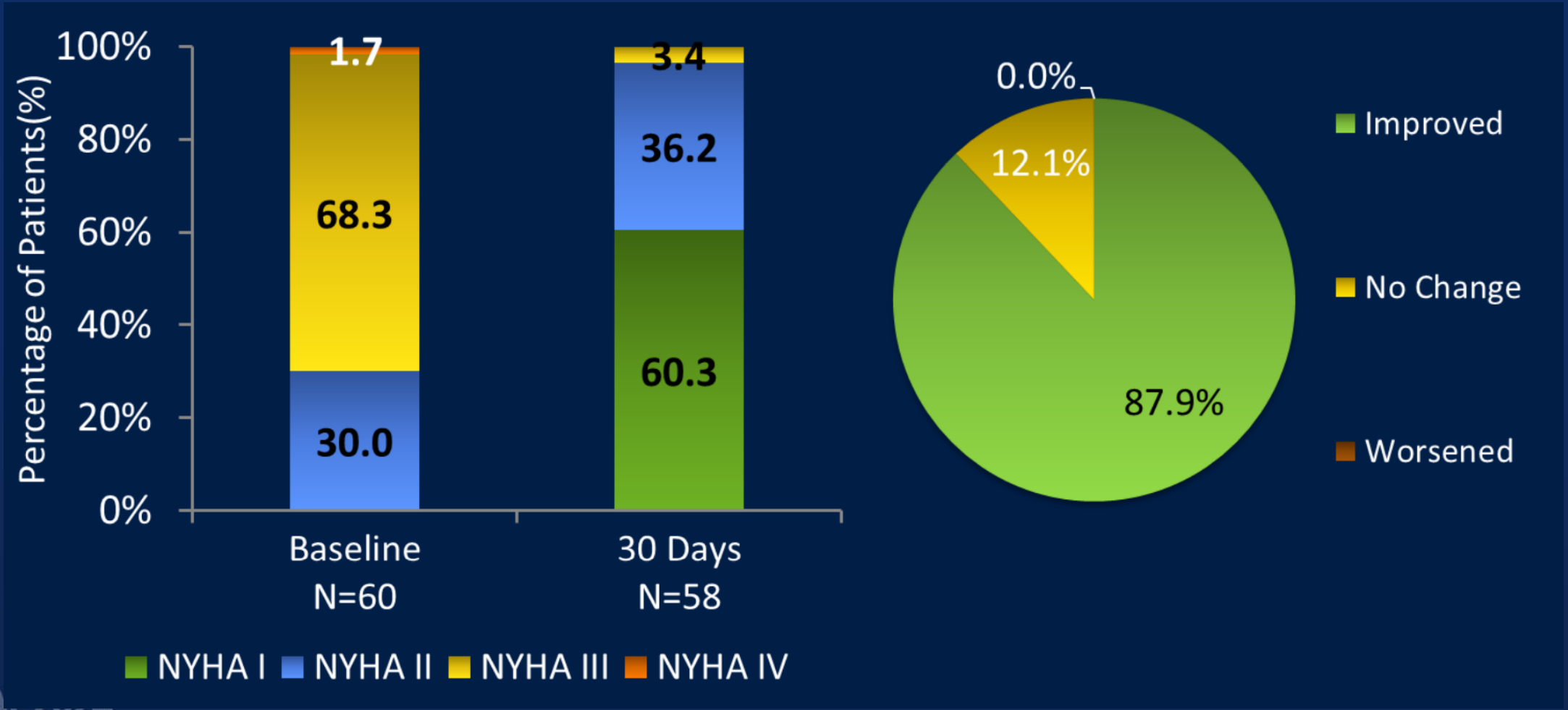

Medtronic

CVRF

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+

**SUPERIOR**
EOAs at 1 year

**Evolut TAVR**
**2.3 cm²**
VS.
**SAVR 2.0 cm²**

**SUPERIOR**
Gradients at 1 year

**Evolut TAVR**
**8.6 mm Hg**
VS.
**SAVR 11.2 mm Hg**



LARGER EOAs

LOWER GRADIENTS

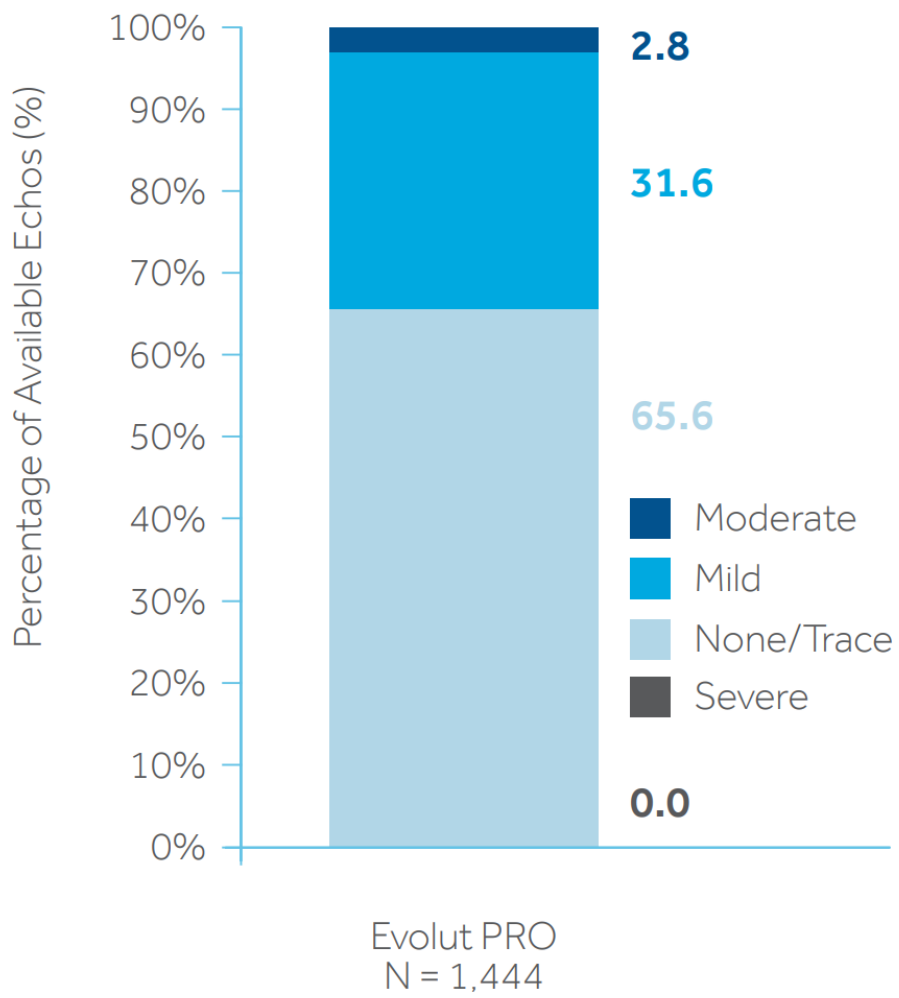
Medtronic



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+

## Total Aortic Regurgitation at 30 Days[6]




## 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

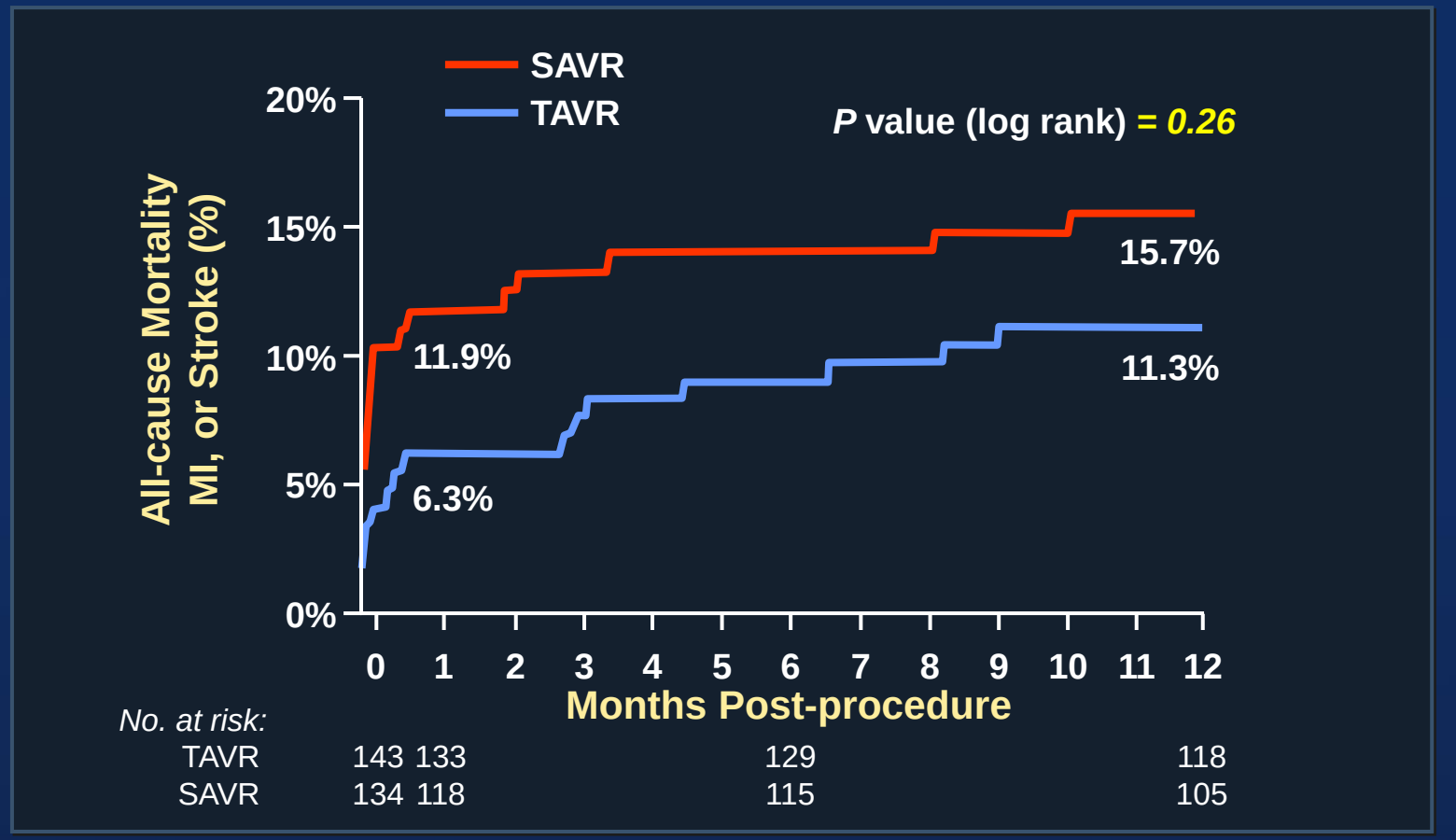
Thyregod HG et al,  J Am Coll Cardiol. 2015 May 26;65(20):2184-94
Lars Søndergaard et al, Circ Cardiovasc Interv. 2016;9:e003665

# 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



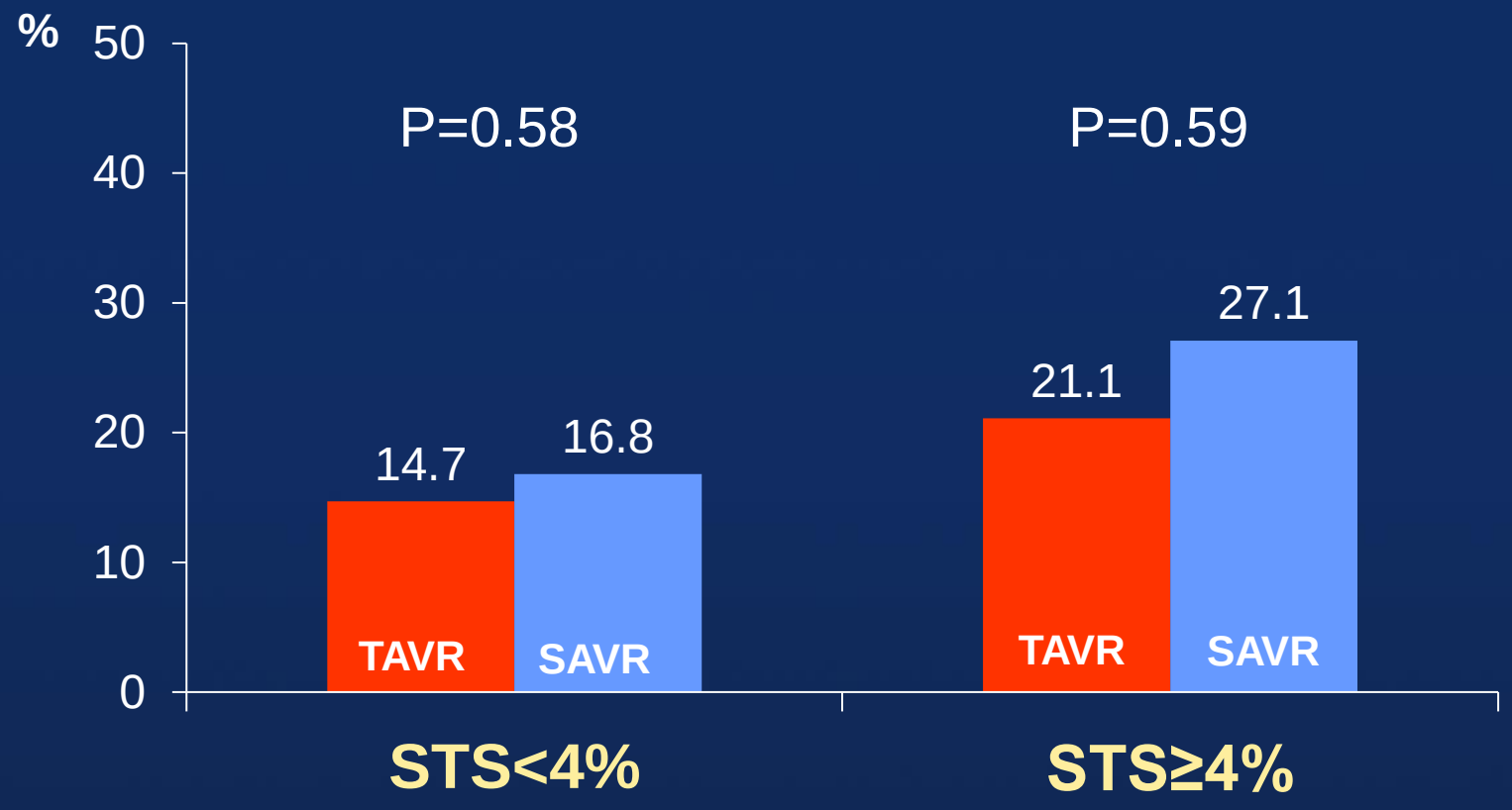

Thyregod HG et al, J Am Coll Cardiol. 2015 May 26;65(20):2184-94
Lars Søndergaard et al, Circ Cardiovasc Interv. 2016;9:e003665

# 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

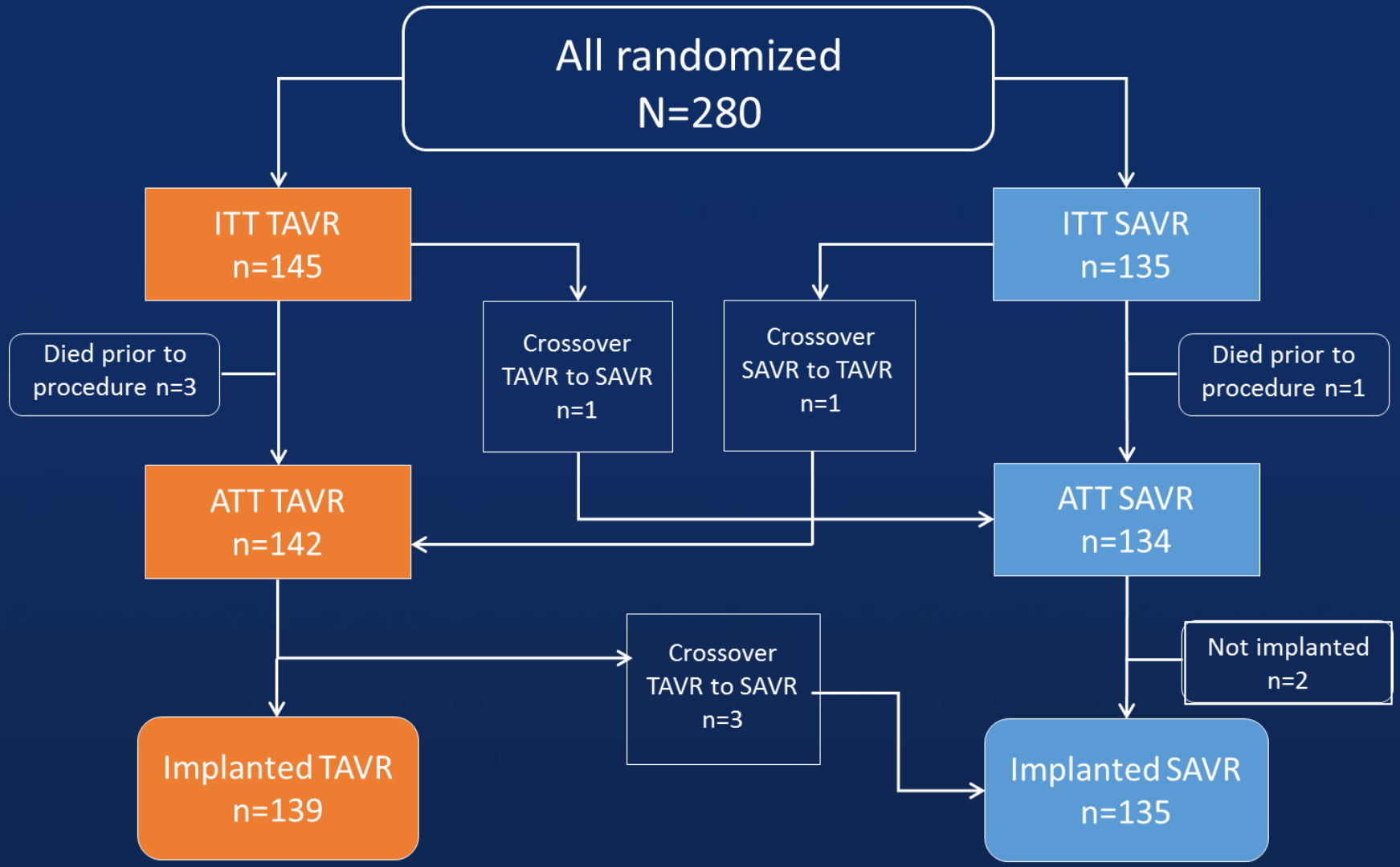
# NOTION Trial

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

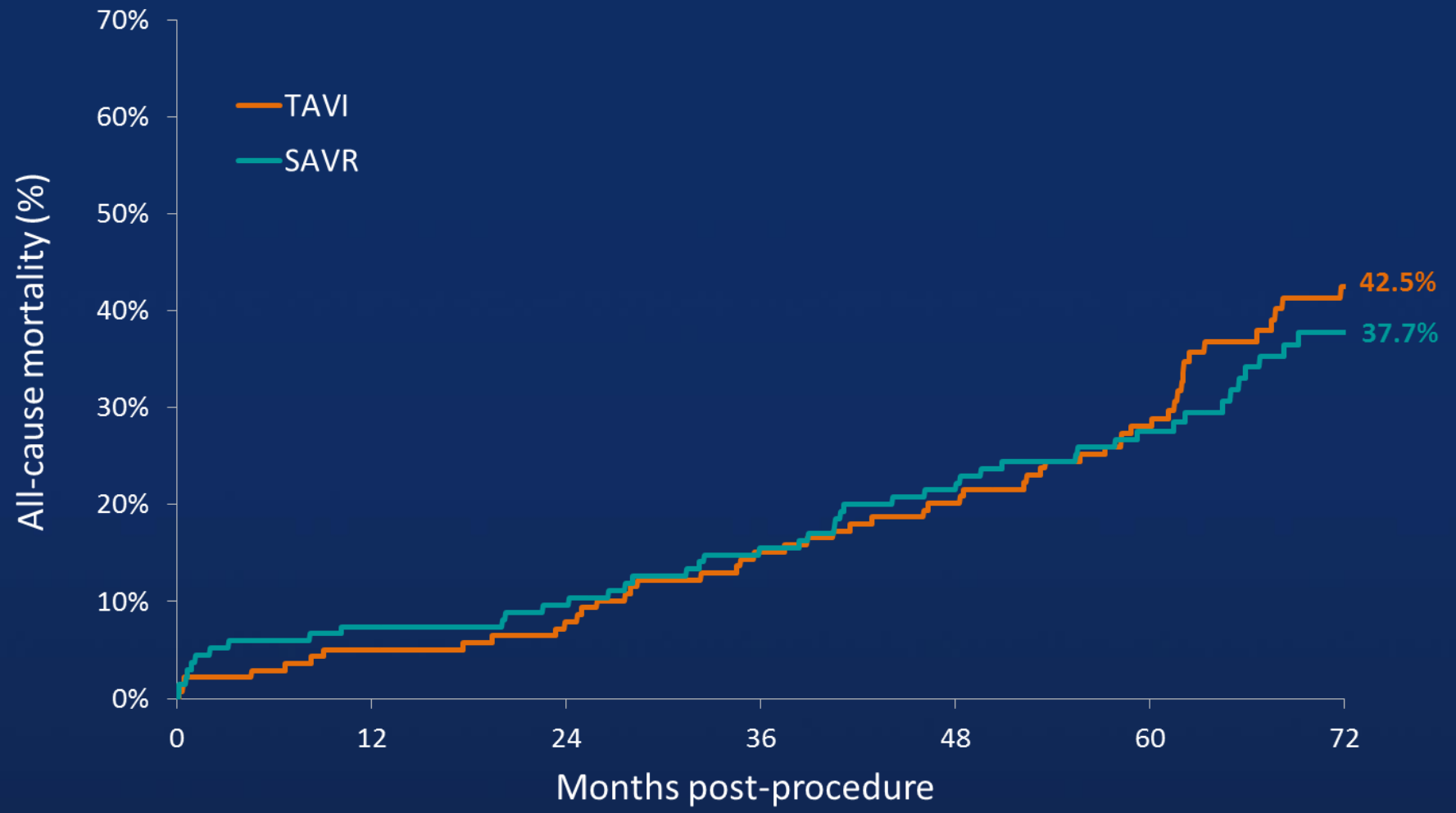
Lars Søndergaard et al, J Am Coll Cardiol. 2019;73:546–53

# NOTION Trial

## Trial Flow



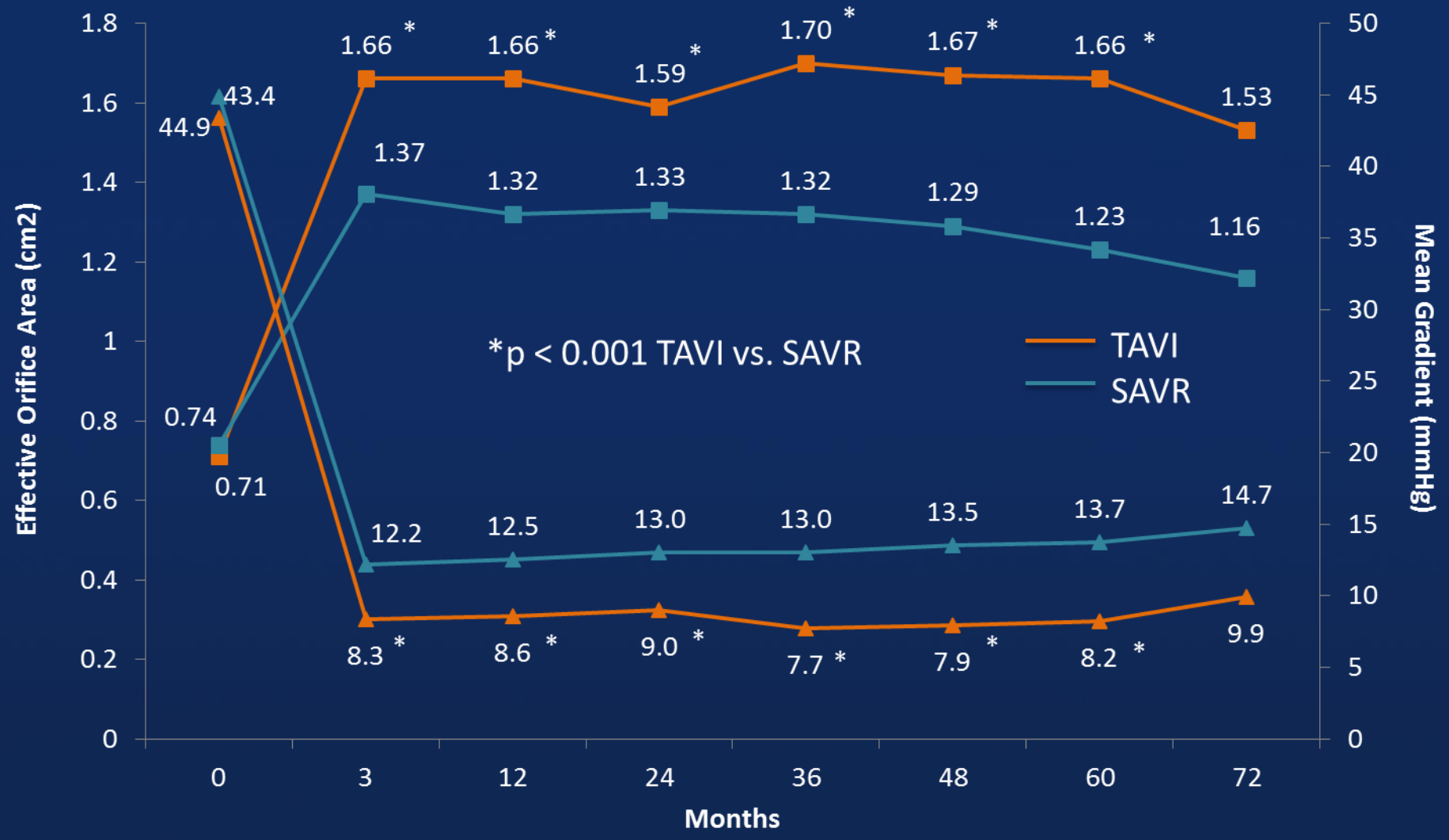
# NOTION Trial: 6 year Results
## All-cause mortality




**Number at risk:**

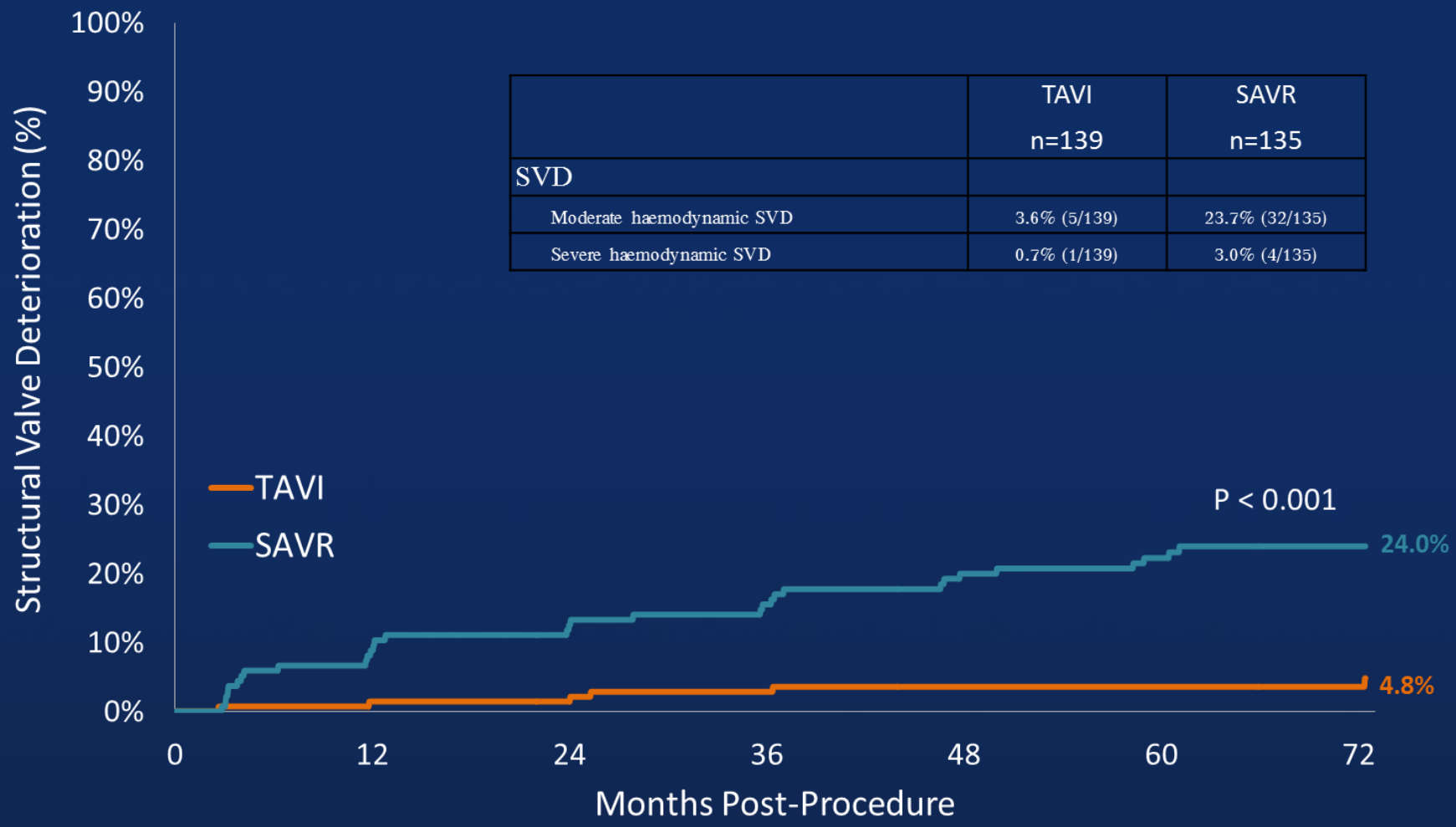
| | | | | | | |
|---|---|---|---|---|---|---|
| 139 136 | 132 | 128 | 118 | 111 | 88 | 46 |
| 135 130 | 125 | 122 | 114 | 104 | 88 | 48 |

# 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 |

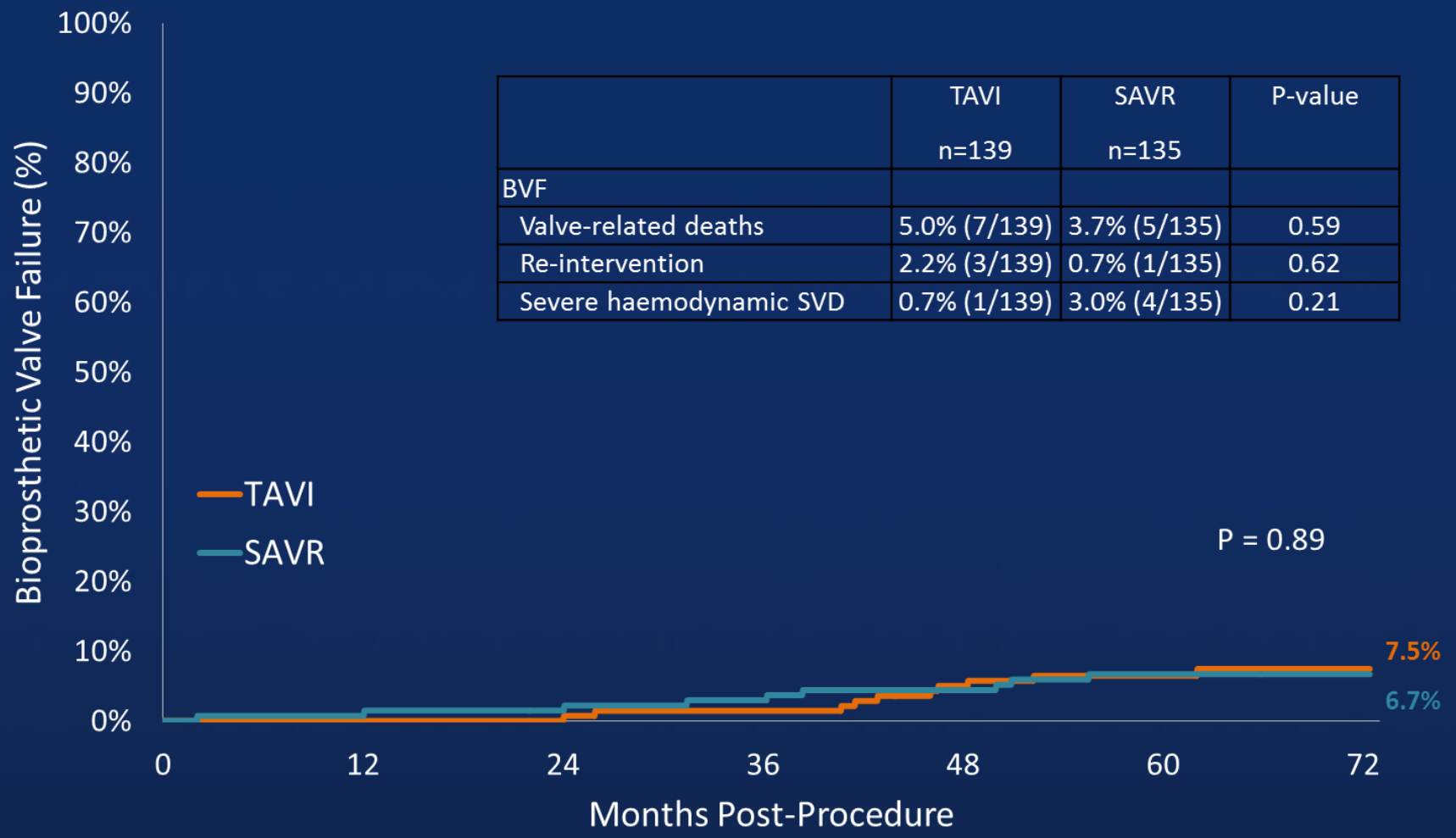
# NOTION Trial
## Durability analysis methods

- 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 |




Number at risk:

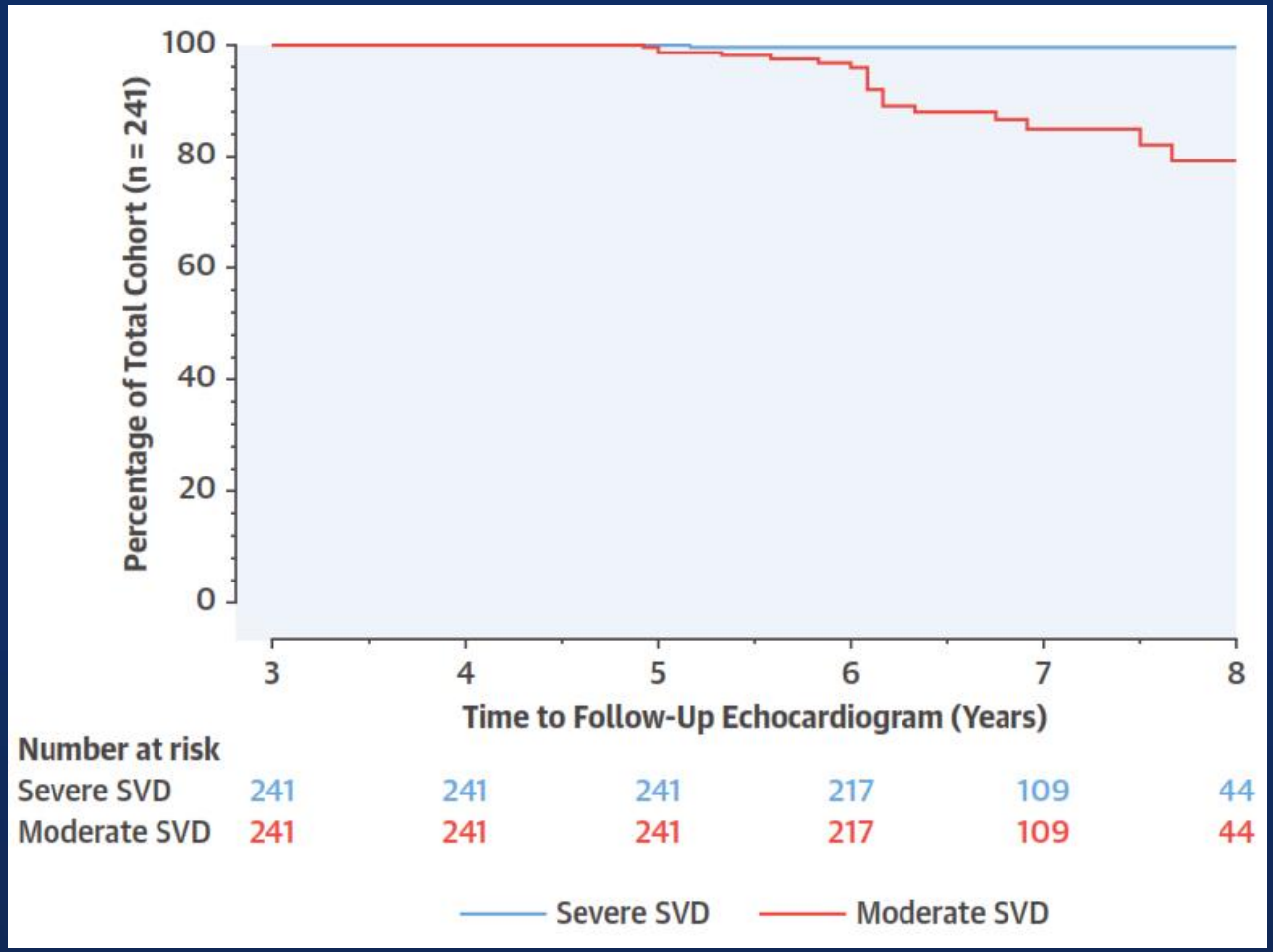
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 139 | 135 | 132 | 127 | 117 | 108 | 86 | 45 |
| 135 | 127 | 125 | 120 | 112 | 101 | 84 | 45 |

# 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

# DEDICATE Trial

## Transcatheter or Surgical Aortic Valve Replacement in Low to Intermediate Risk Patients with Symptomatic Aortic Stenosis

# DEDICATE Trial

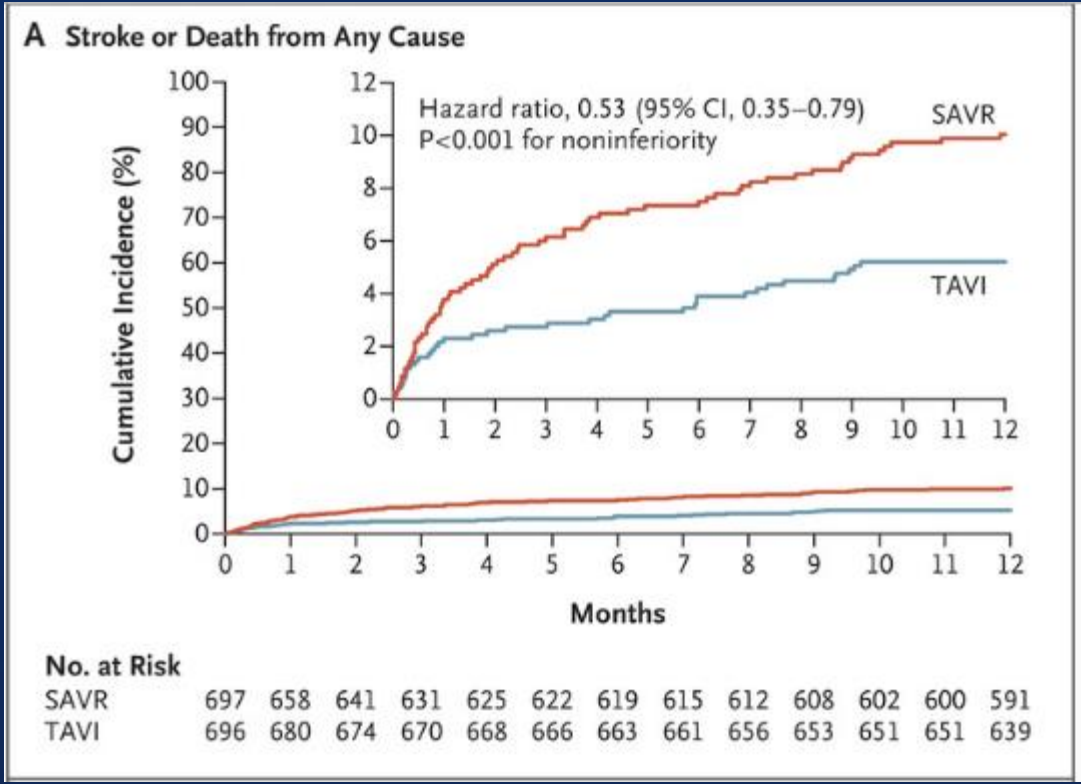


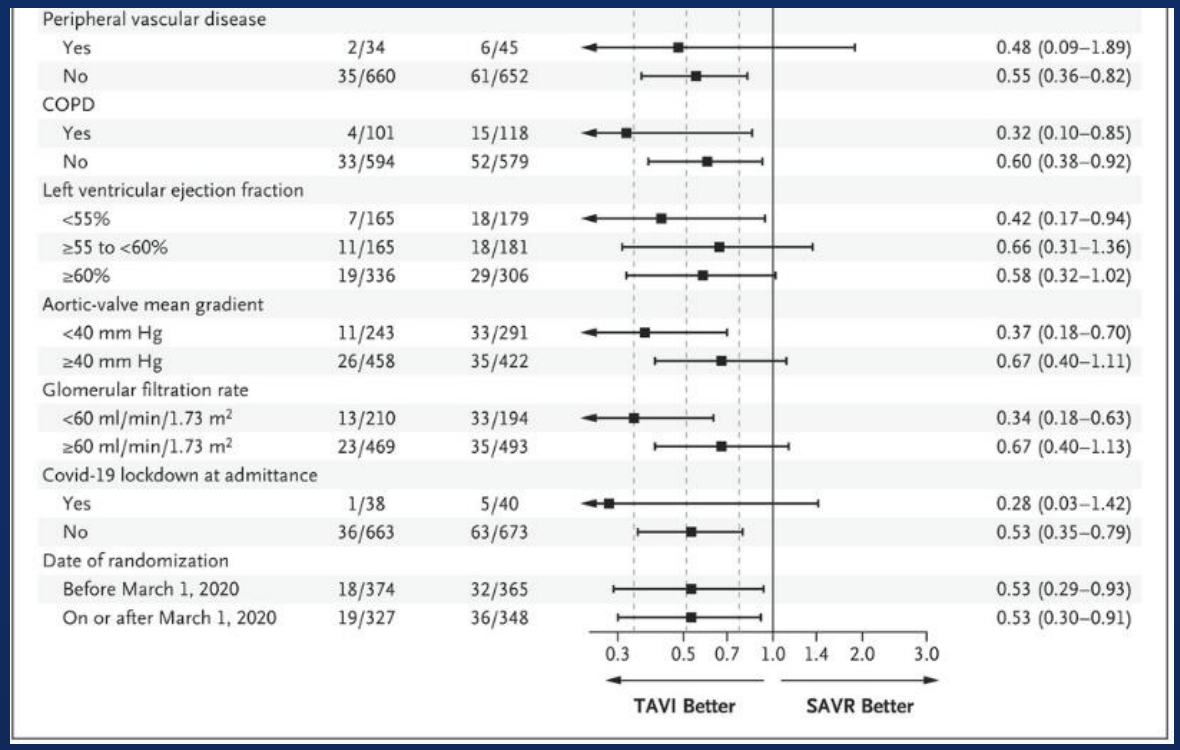

**Table 2.** Primary and Secondary Outcomes at 1 Year (Intention-to-Treat Population).*

| Outcome | TAVI (N=701) | | SAVR (N=713) | | Hazard Ratio (95% CI) |
|---|---|---|---|---|---|
| | *no. of events* | *% of patients* | *no. of events* | *% of patients* | |
| **Primary outcome** | | | | | |
| Death from any cause or stroke† | 37 | 5.4 | 68 | 10.0 | 0.53 (0.35–0.79) |
| **Secondary outcomes** | | | | | |
| Death from any cause | 18 | 2.6 | 42 | 6.2 | 0.43 (0.24–0.73) |
| Stroke | 20 | 2.9 | 32 | 4.7 | 0.61 (0.35–1.06) |
| Stroke or TIA | 28 | 4.1 | 35 | 5.1 | 0.78 (0.47–1.27) |
| Disabling stroke | 9 | 1.3 | 21 | 3.1 | 0.42 (0.19–0.88) |
| Death from any cause or disabling stroke | 26 | 3.8 | 57 | 8.4 | 0.45 (0.28–0.70) |
| Cardiovascular death | 14 | 2.0 | 30 | 4.4 | 0.47 (0.24–0.86) |
| Myocardial infarction | 7 | 1.0 | 14 | 2.1 | 0.51 (0.20–1.19) |
| New-onset atrial fibrillation | 86 | 12.4 | 211 | 30.8 | 0.36 (0.28–0.46) |
| New-onset left bundle-branch block | 222 | 32.0 | 120 | 17.5 | 2.03 (1.63–2.54) |
| New permanent pacemaker implantation | 82 | 11.8 | 47 | 6.7 | 1.81 (1.27–2.61) |
| Prosthetic-valve dysfunction | 11 | 1.6 | 4 | 0.6 | 2.44 (0.87–8.15) |
| Prosthetic-valve endocarditis | 4 | 0.6 | 7 | 0.9 | 0.66 (0.18–2.19) |
| Prosthetic-valve thrombosis | 5 | 0.7 | 2 | 0.3 | 2.09 (0.50–11.64) |
| Aortic-valve reintervention | 4 | 0.6 | 2 | 0.3 | 1.70 (0.38–9.78) |
| Major or life-threatening or disabling bleeding | 30 | 4.3 | 119 | 17.2 | 0.24 (0.16–0.35) |
| Acute kidney injury of stage II or III‡ | 9 | 1.3 | 17 | 2.5 | 0.56 (0.24–1.21) |
| Vascular access-site complication | 55 | 7.9 | 5 | 0.7 | 10.64 (4.84–28.94) |
| Rehospitalization for cardiovascular cause | 84 | 12.2 | 91 | 13.3 | 0.89 (0.66–1.20) |

* The analyses were stratified according to the STS-PROM score. The percentage of patients was calculated as a Kaplan–Meier estimate. The 95% confidence intervals have not been adjusted for multiplicity and should not be used to make hypothesis-test inferences about superiority or noninferiority. TIA denotes transient ischemic attack.
† P<0.001 for the primary analysis.
‡ Acute kidney injury was adjudicated according to Valve Academic Research Consortium 2 criteria within 7 days after the index procedure.

# DEDICATE Trial

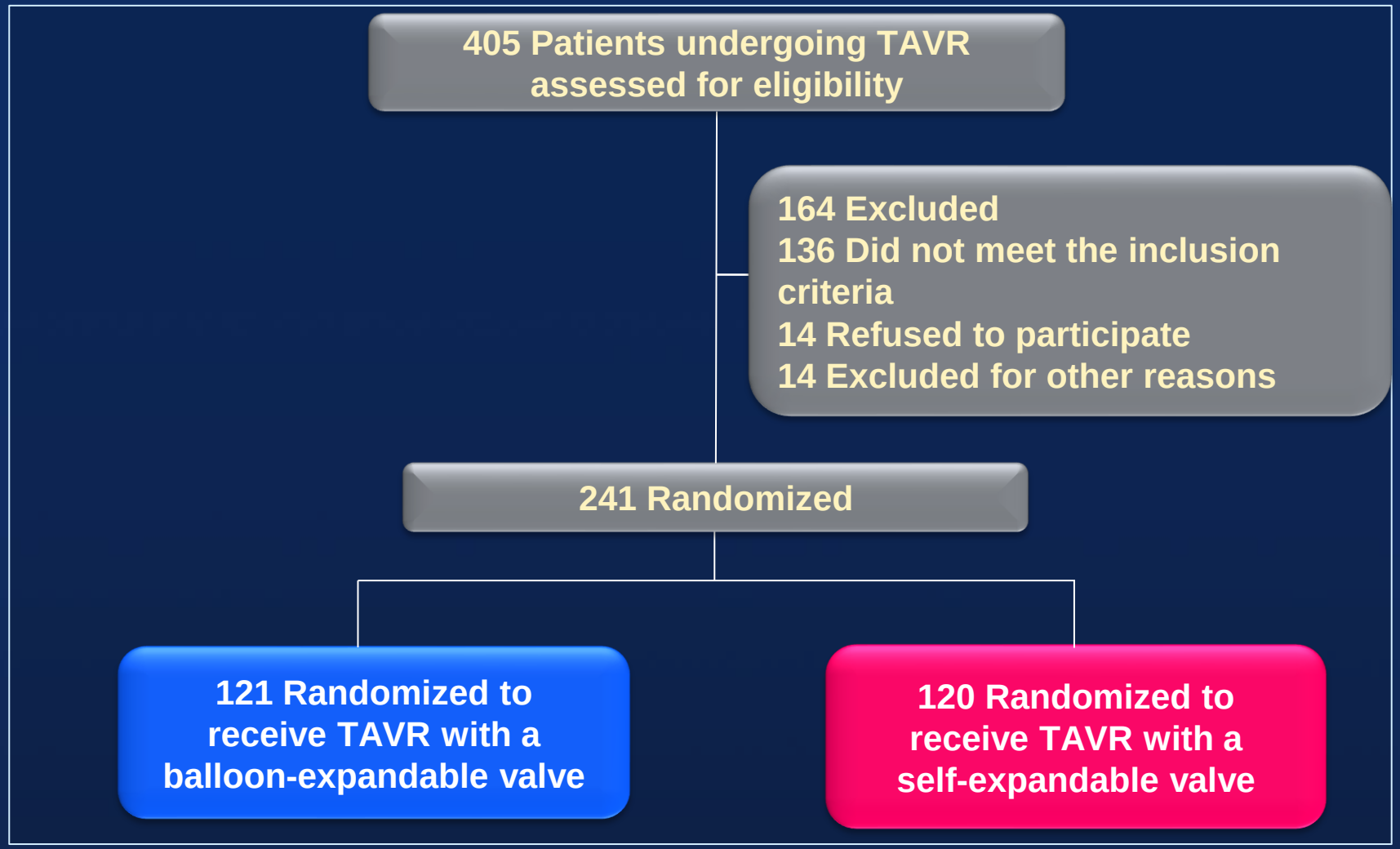
| Subgroup | TAVI | SAVR | Hazard Ratio for Death or Stroke (95% CI) |
|---|---|---|---|
| | *no. of patients with event/total no.* | | |
| Overall | 37/701 | 68/713 | 0.53 (0.35–0.79) |
| Age | | | |
| <75 yr | 18/359 | 30/345 | 0.56 (0.31–0.98) |
| ≥75 yr | 19/337 | 38/354 | 0.51 (0.29–0.87) |
| Sex | | | |
| Male | 21/390 | 35/400 | 0.60 (0.35–1.02) |
| Female | 16/306 | 33/298 | 0.46 (0.25–0.81) |
| Body-mass index | | | |
| <25 | 8/163 | 17/159 | 0.46 (0.19–1.01) |
| 25 to <30 | 12/277 | 26/293 | 0.48 (0.24–0.92) |
| ≥30 | 17/255 | 25/246 | 0.63 (0.34–1.15) |
| STS-PROM score | | | |
| ≤2% | 15/387 | 23/378 | 0.62 (0.32–1.18) |
| >2 to ≤4% | 18/282 | 36/284 | 0.49 (0.27–0.84) |
| >4% | 4/27 | 9/35 | 0.53 (0.15–1.55) |
| NYHA class | | | |
| ≤2 | 20/374 | 30/379 | 0.66 (0.37–1.16) |
| >2 | 17/321 | 38/318 | 0.42 (0.23–0.73) |
| Coronary artery disease | | | |
| Yes | 15/238 | 26/266 | 0.62 (0.32–1.14) |
| No | 22/456 | 42/431 | 0.48 (0.28–0.80) |
| Previous myocardial infarction | | | |
| Yes | 1/36 | 7/52 | 0.27 (0.03–1.23) |
| No | 36/660 | 61/645 | 0.56 (0.37–0.83) |
| Previous stroke | | | |
| Yes | 2/42 | 5/42 | 0.44 (0.08–1.82) |
| No | 35/650 | 62/654 | 0.55 (0.36–0.82) |
| Cerebrovascular disease | | | |
| Yes | 2/27 | 6/31 | 0.42 (0.08–1.63) |
| No | 35/649 | 60/662 | 0.57 (0.38–0.86) |
| Peripheral vascular disease | | | |
| Yes | 2/34 | 6/45 | 0.48 (0.09–1.89) |
| No | 35/660 | 61/652 | 0.55 (0.36–0.82) |
| COPD | | | |
| Yes | 4/101 | 15/118 | 0.32 (0.10–0.85) |
| No | 33/594 | 52/579 | 0.60 (0.38–0.92) |
| Left ventricular ejection fraction | | | |
| <55% | 7/165 | 18/179 | 0.42 (0.17–0.94) |
| ≥55 to <60% | 11/165 | 18/181 | 0.66 (0.31–1.36) |
| ≥60% | 19/336 | 29/306 | 0.58 (0.32–1.02) |
| Aortic-valve mean gradient | | | |
| <40 mm Hg | 11/243 | 33/291 | 0.37 (0.18–0.70) |
| ≥40 mm Hg | 26/458 | 35/422 | 0.67 (0.40–1.11) |
| Glomerular filtration rate | | | |
| <60 ml/min/1.73 m² | 13/210 | 33/194 | 0.34 (0.18–0.63) |
| ≥60 ml/min/1.73 m² | 23/469 | 35/493 | 0.67 (0.40–1.13) |
| Covid-19 lockdown at admittance | | | |
| Yes | 1/38 | 5/40 | 0.28 (0.03–1.42) |
| No | 36/663 | 63/673 | 0.53 (0.35–0.79) |
| Date of randomization | | | |
| Before March 1, 2020 | 18/374 | 32/365 | 0.53 (0.29–0.93) |
| On or after March 1, 2020 | 19/327 | 36/348 | 0.53 (0.30–0.91) |



# 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 |

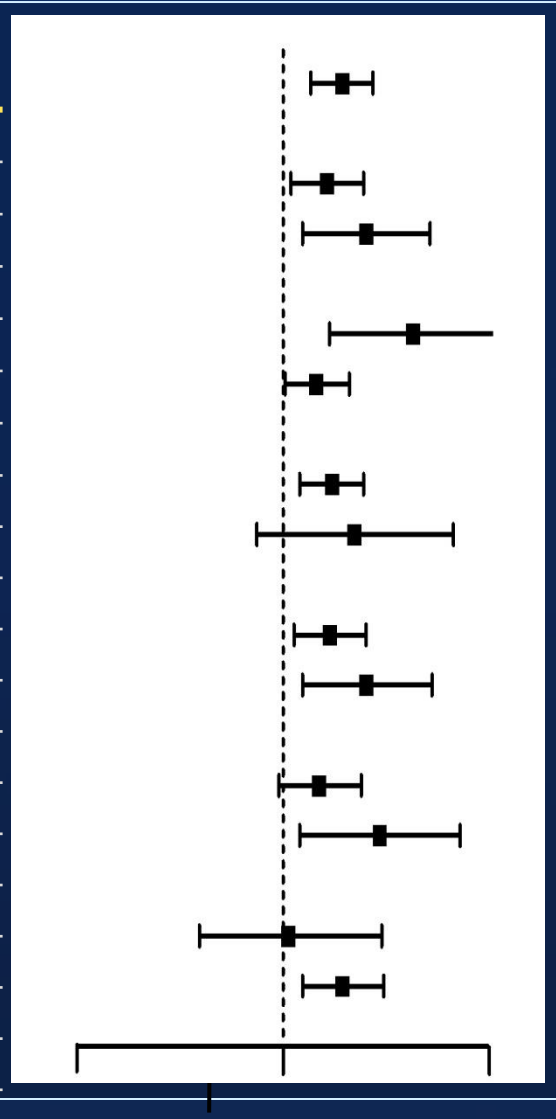
Adams DH, Popma JJ, Reardon MJ, et al. New Engl J Med 2014; Mar 29, [Epub ahead of print]

# 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 |

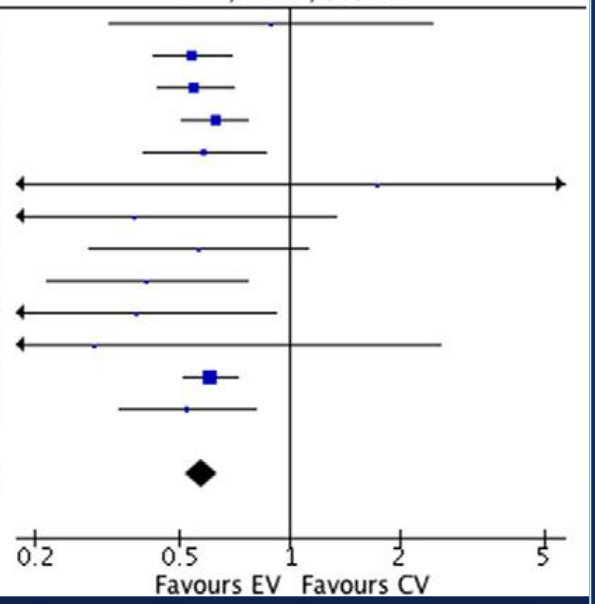
# CoreValve vs. SAPIEN XT

## 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: $Z = 11.42$ ($P < 0.00001$)



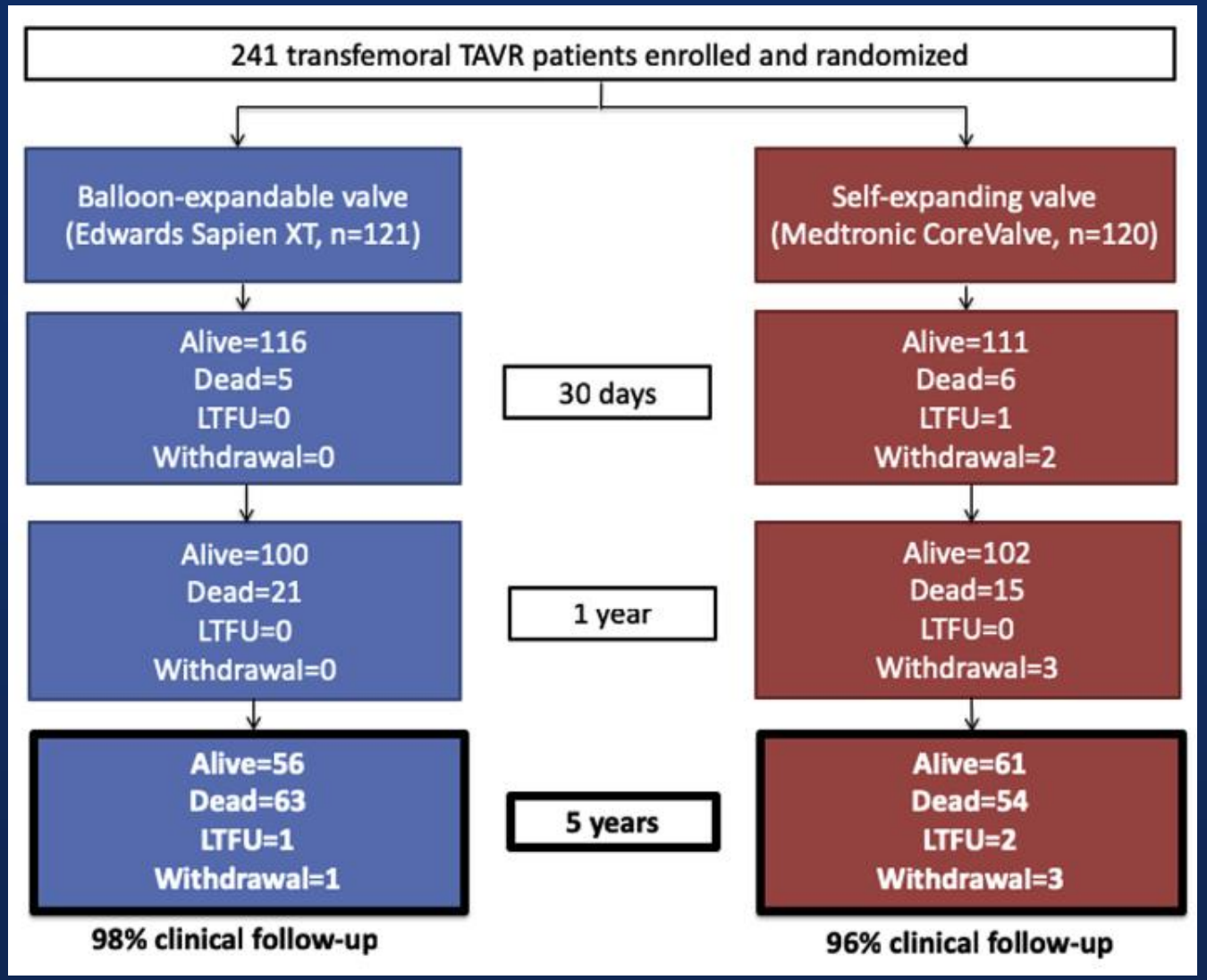

**Conclusion:** **CoreValve is associated with higher incidence of post-TAVR moderate to severe paravalvular AR.**

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 |

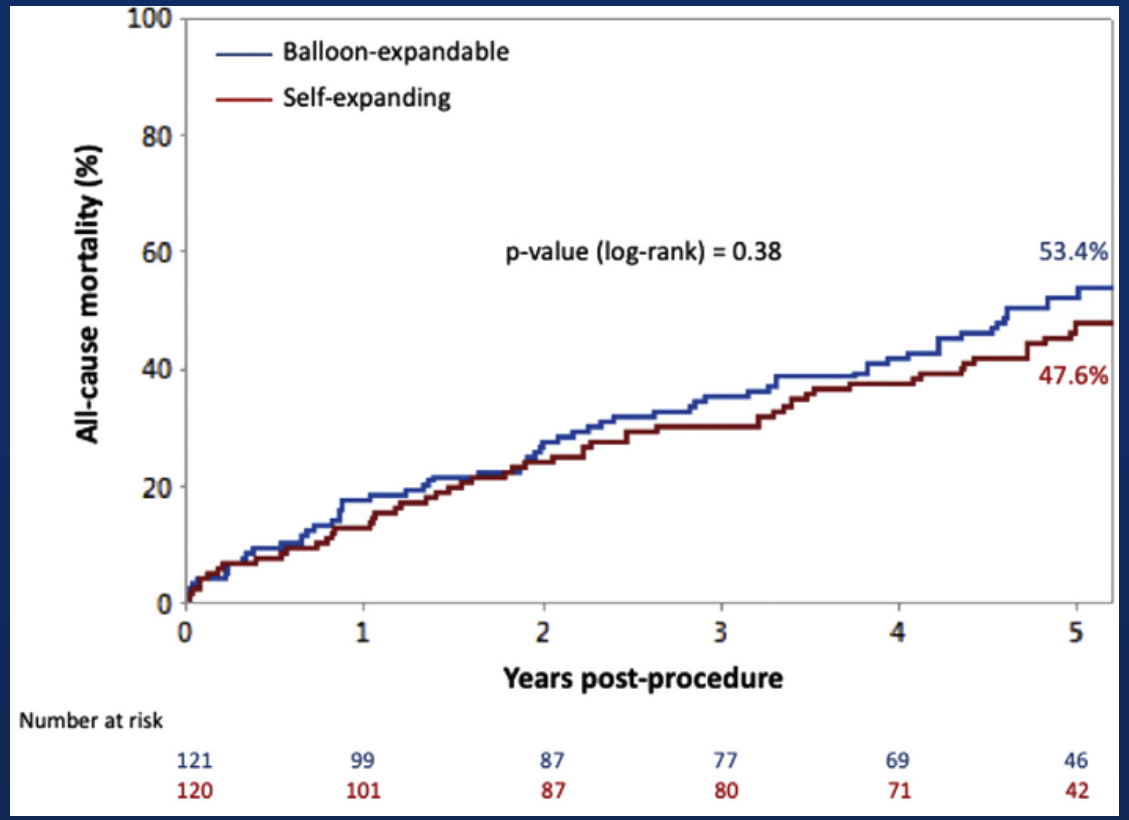




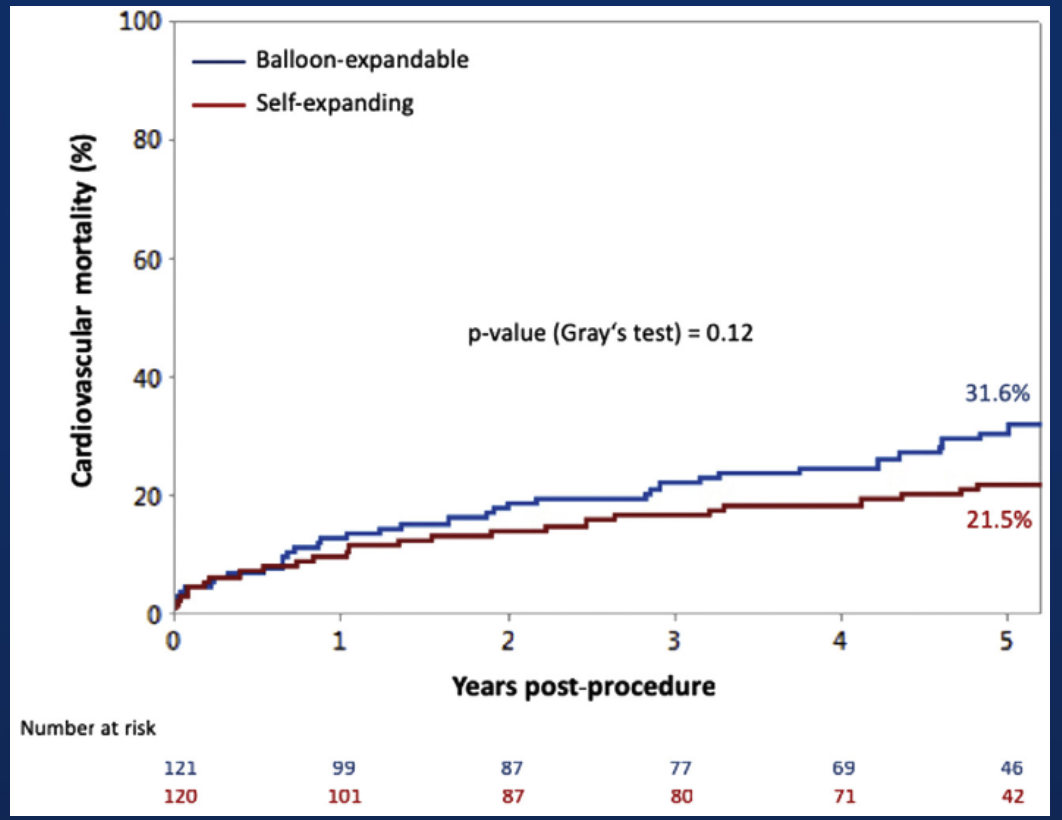
Abdel-Wahab, M. et al. J Am Coll Cardiol Intv. 2020;13(9):1071–82.

# 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.

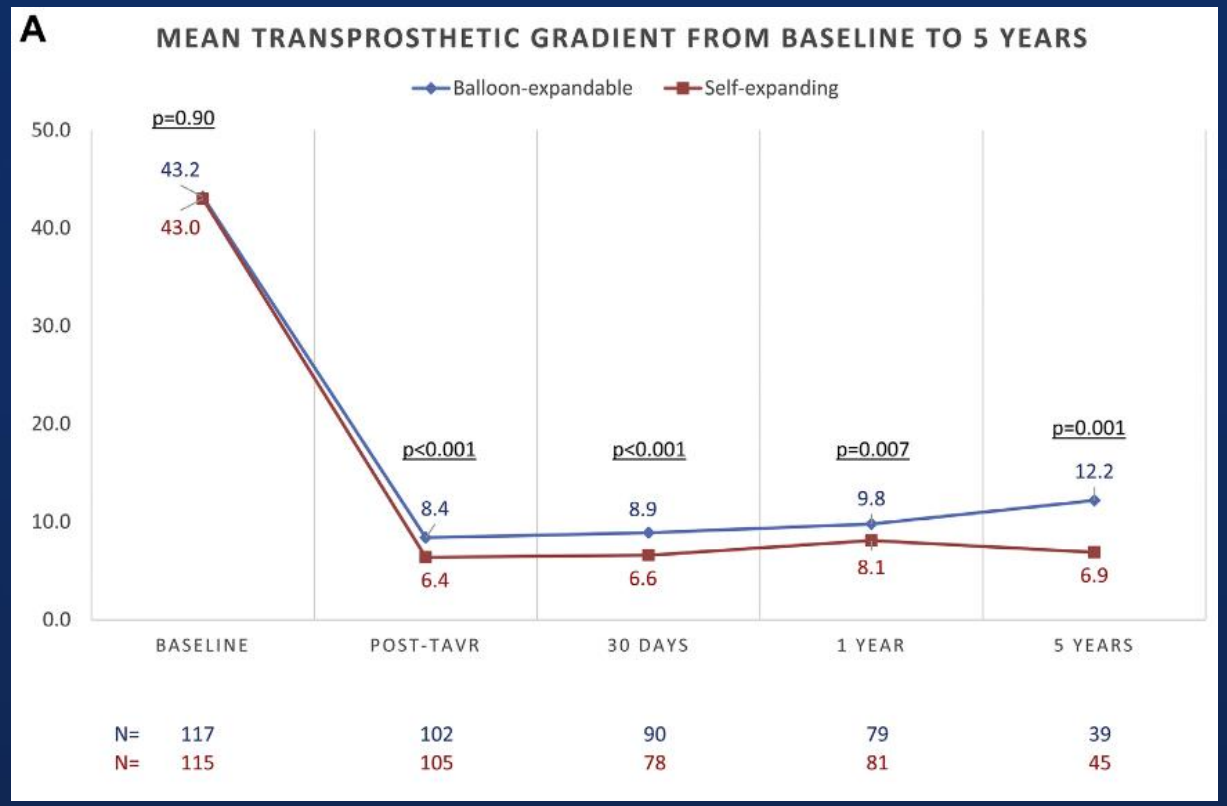
# CHOICE Trial
# 5-Year Outcomes
## Echocardiographic F/U at 5 years

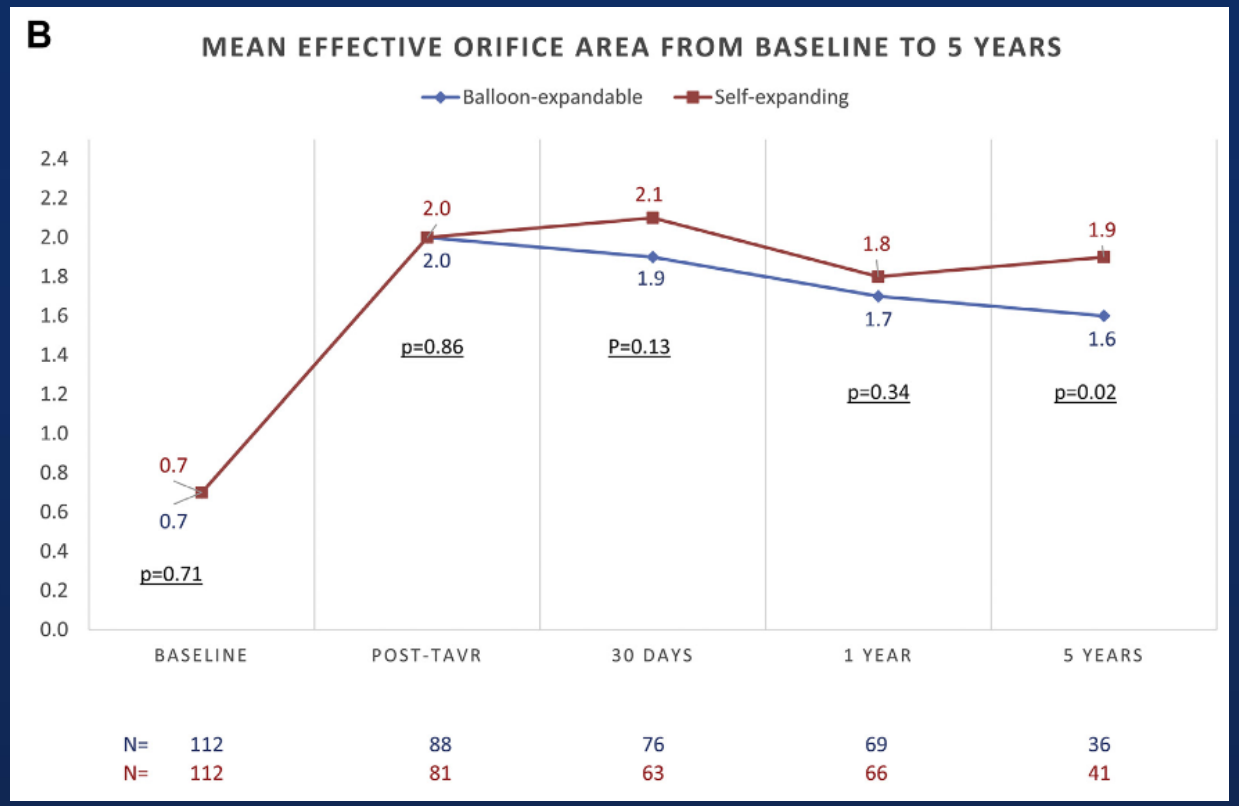
| | Balloon-Expandable Valve (n = 36) | Self-Expanding Valve (n = 41) | p Value |
|---|---|---|---|
| Effective orifice area, $cm^2$ | 1.6 ± 0.5 | 1.9 ± 0.5 | 0.02 |
| Number of patients | 39 | 45 | |
| Mean gradient, mm Hg | 12.2 ± 8.7 | 6.9 ± 2.7 | 0.001 |
| Number of patients | 47 | 52 | |
| Transvalvular 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



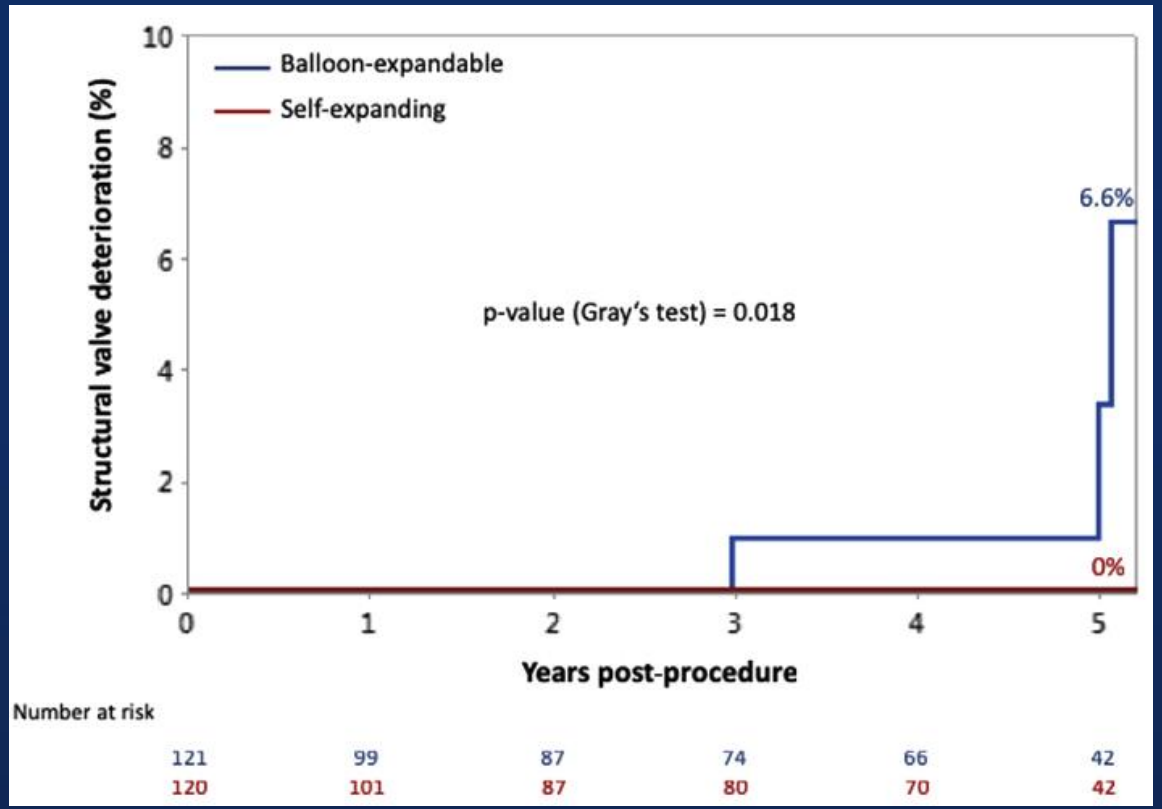



Abdel-Wahab, M. et al. J Am Coll Cardiol Intv. 2020;13(9):1071–82.

# 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.

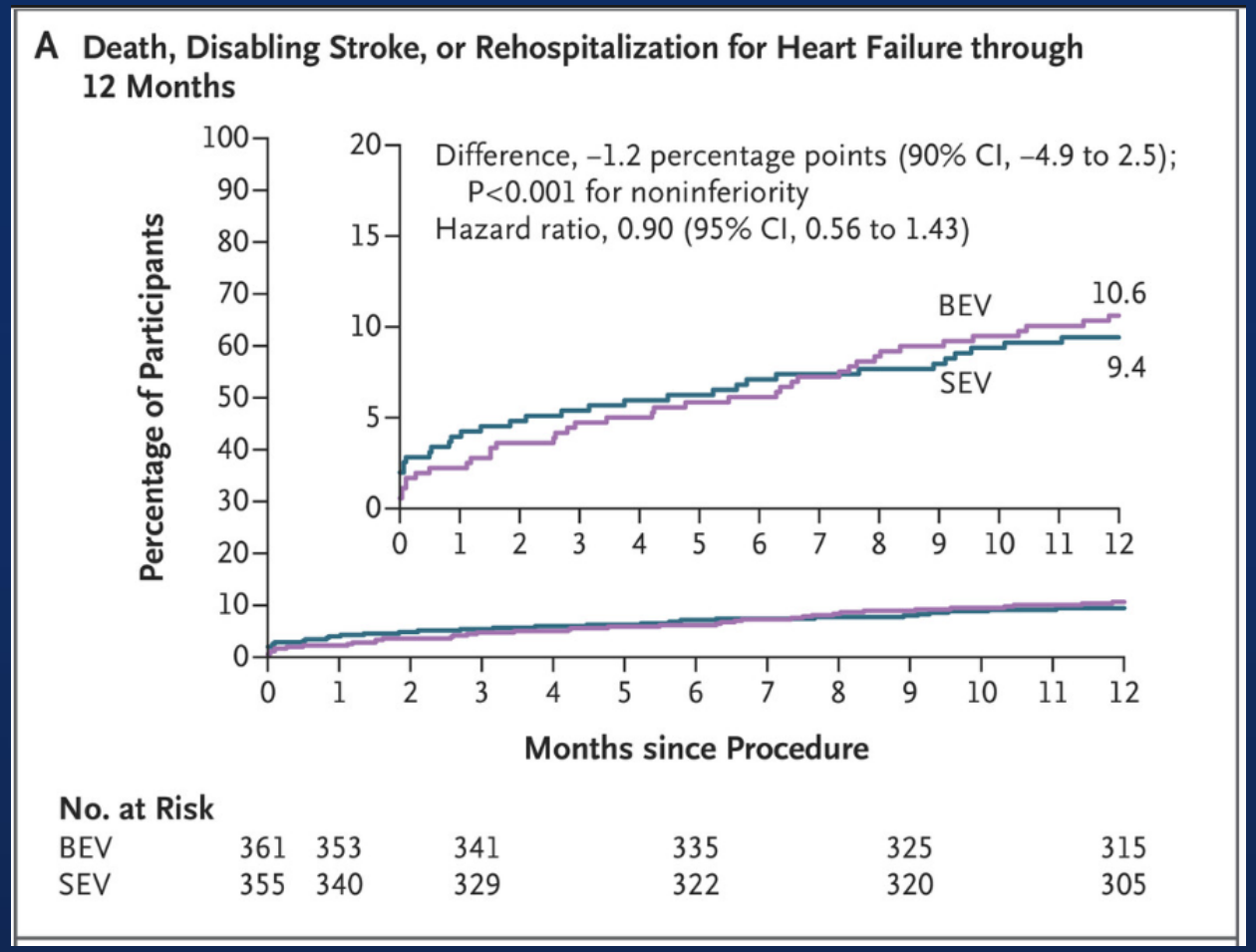
# CoreValve vs. Edwards SAPIEN 3/3U

# SMART TRIAL

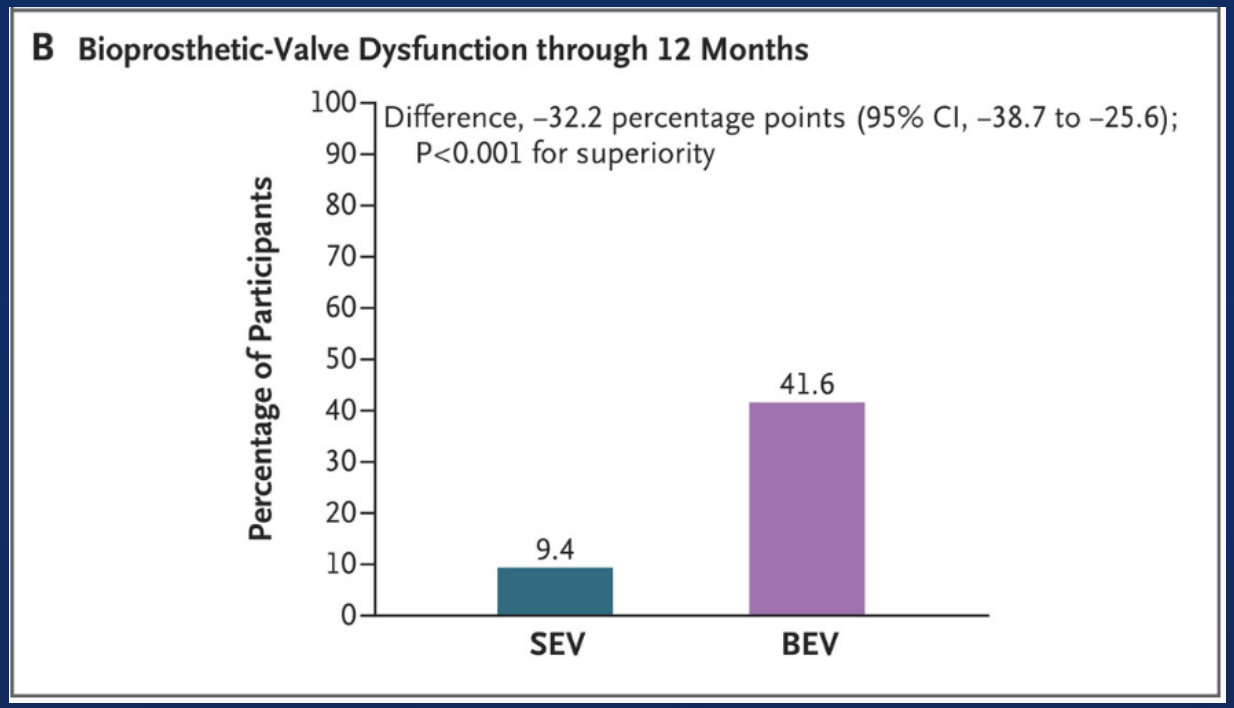
# SMART Trial

Patients had to have an
Aortic valve annulus area of 430mm2 or less.
Suitable anatomy for transfemoral TAVR

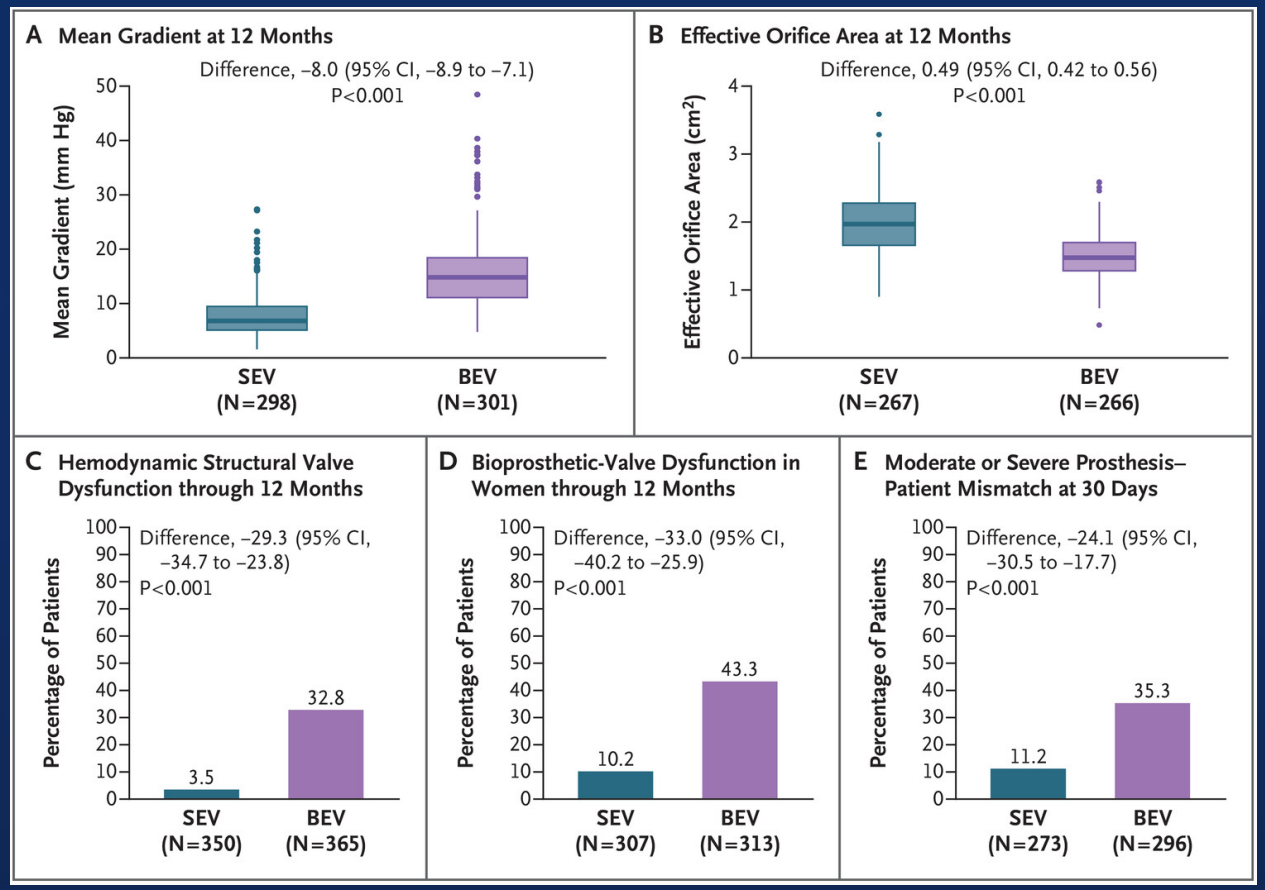
Randomly assigned in a 1:1 ratio to receive
Self-Expanding Evolut PRO/PRO+/FX(Medtronic)
or Balloon-Expandable SAPIEN3/3 Ultra
(Edwards Lifesciences)



# SMART Trial




SEV : Self-Expandable Valve
BEV : Balloon-Expandable Valve



# 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 |

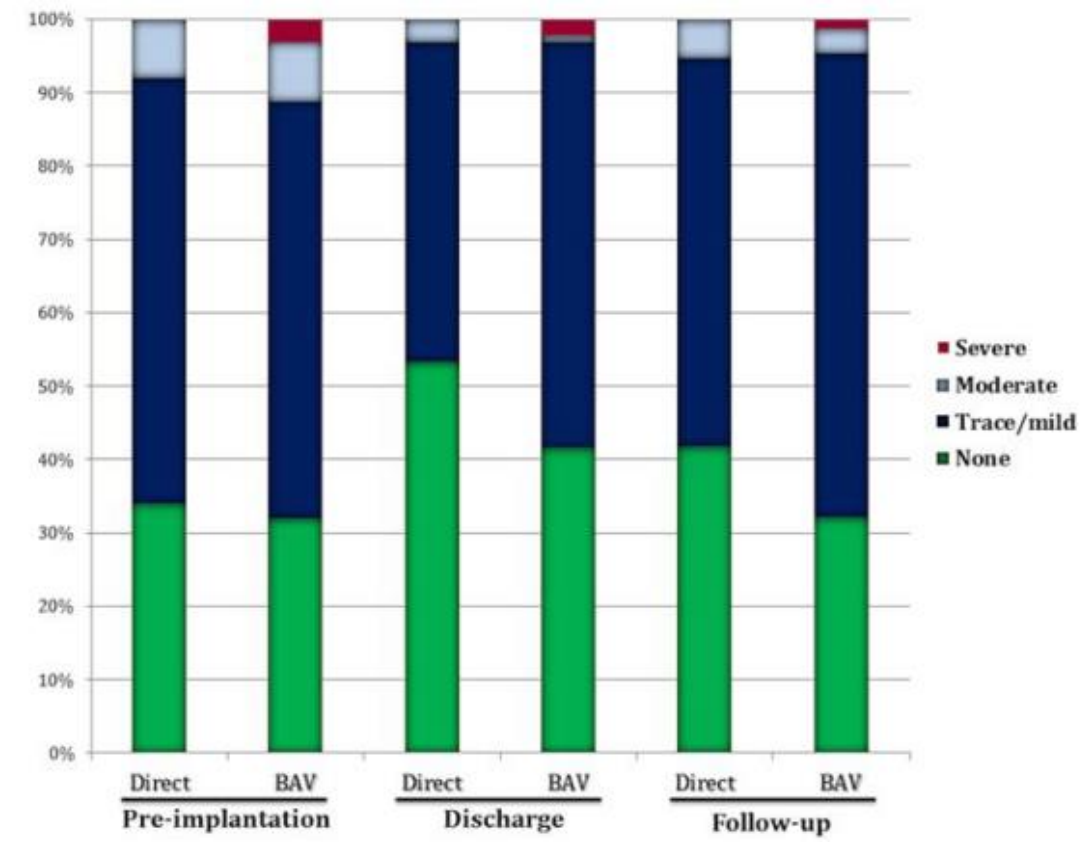
Ferrera C, et al. Cath Cardiovasc Int 2016 online publication

# 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

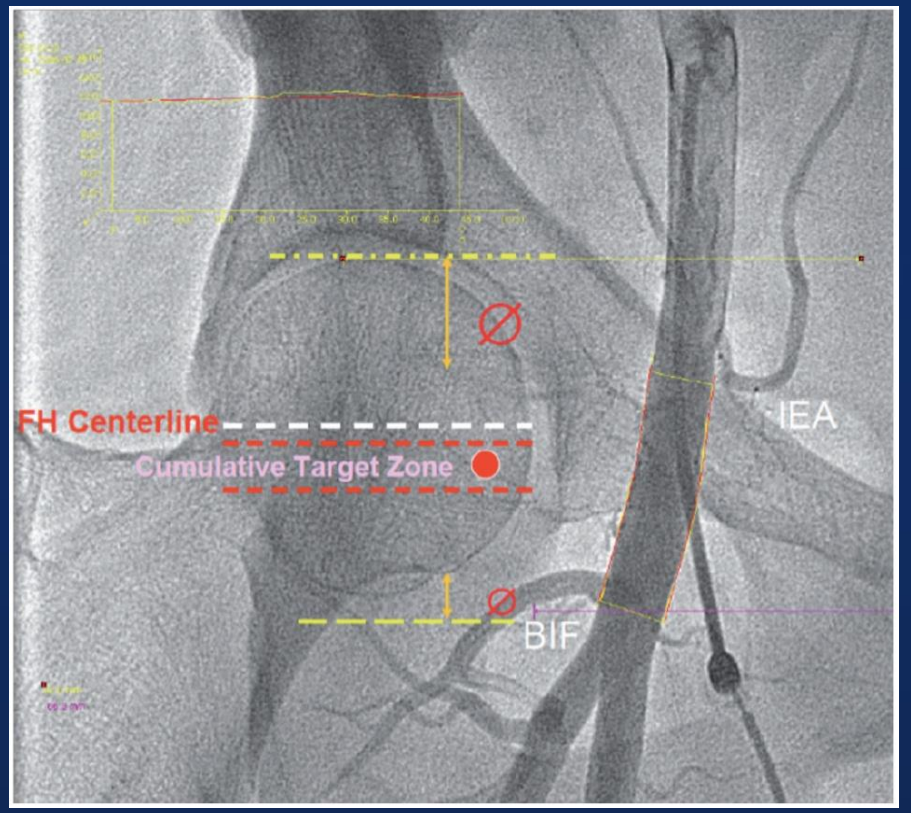
# Clinical outcomes at 12 months

| 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

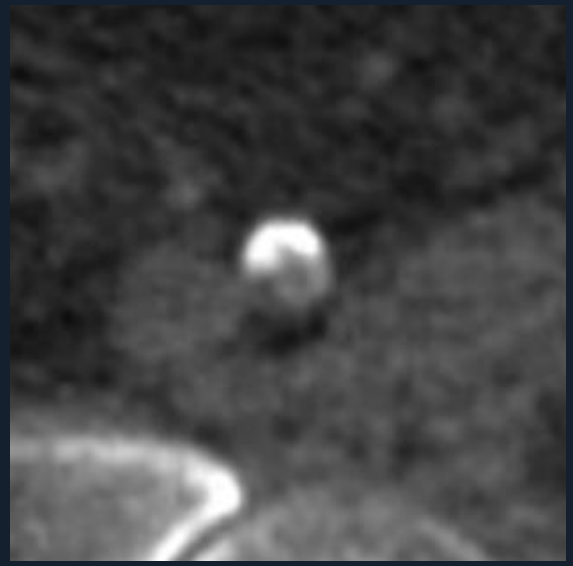
# TAVR
# Vascular Closure Device

# Puncture Site

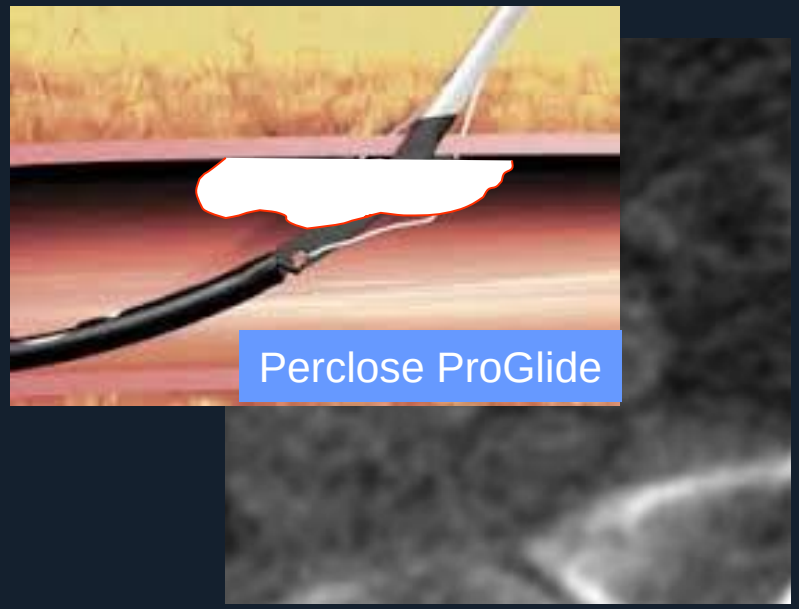


# Puncture Site

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

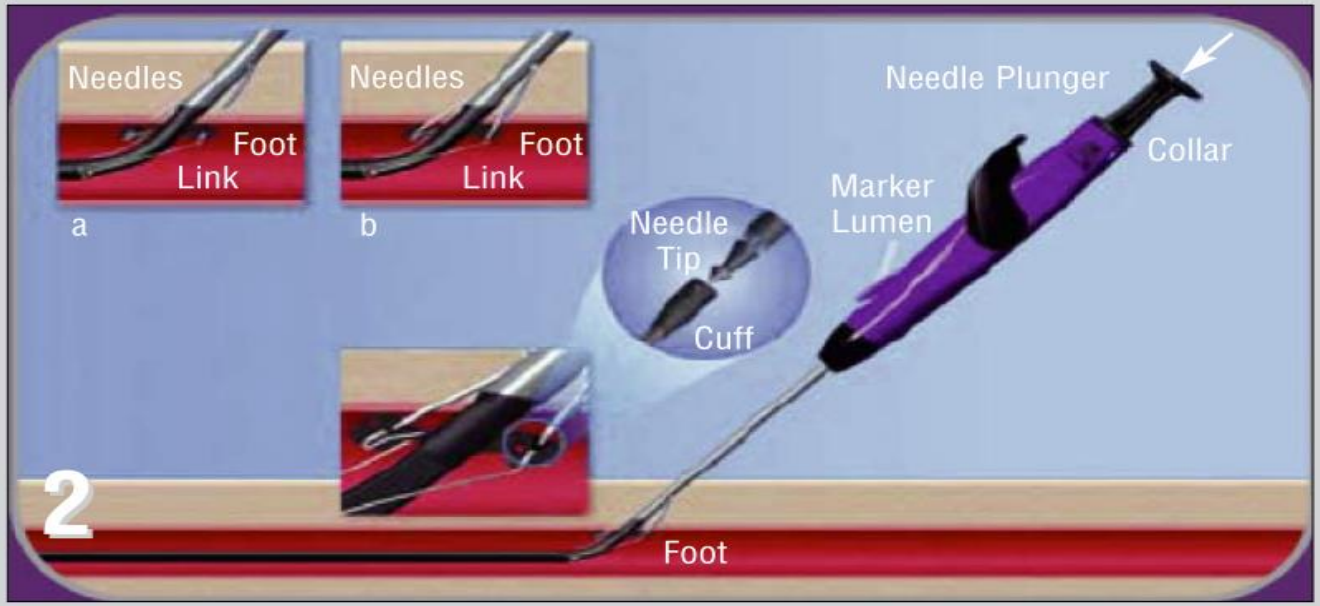
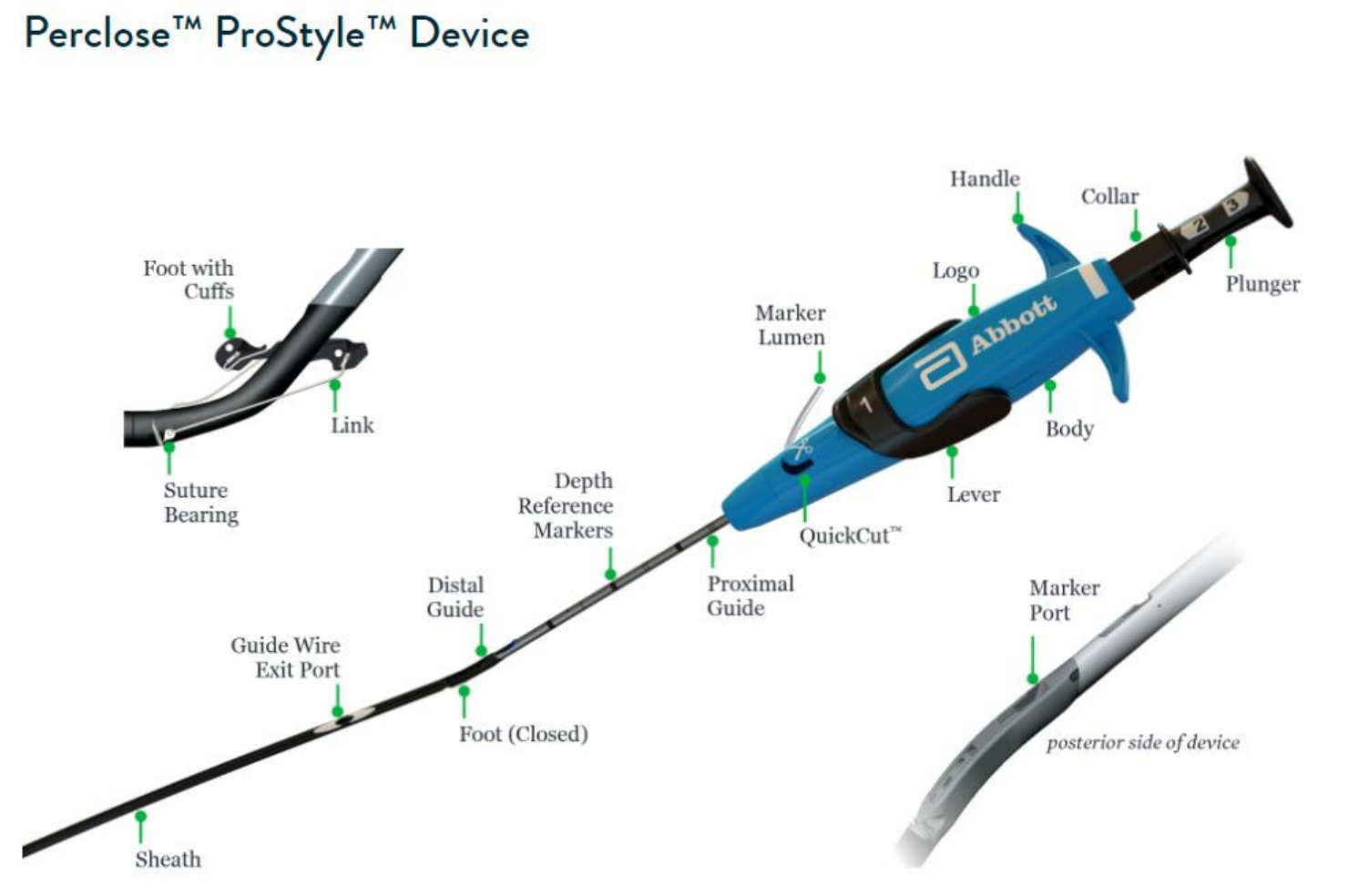



**Figure 1** Perclose ProGlide Suture-Mediated Closure System: needle deployment.
Reprinted from Perclose ProGlide Suture-Mediated Closure System,[21] with permission.

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

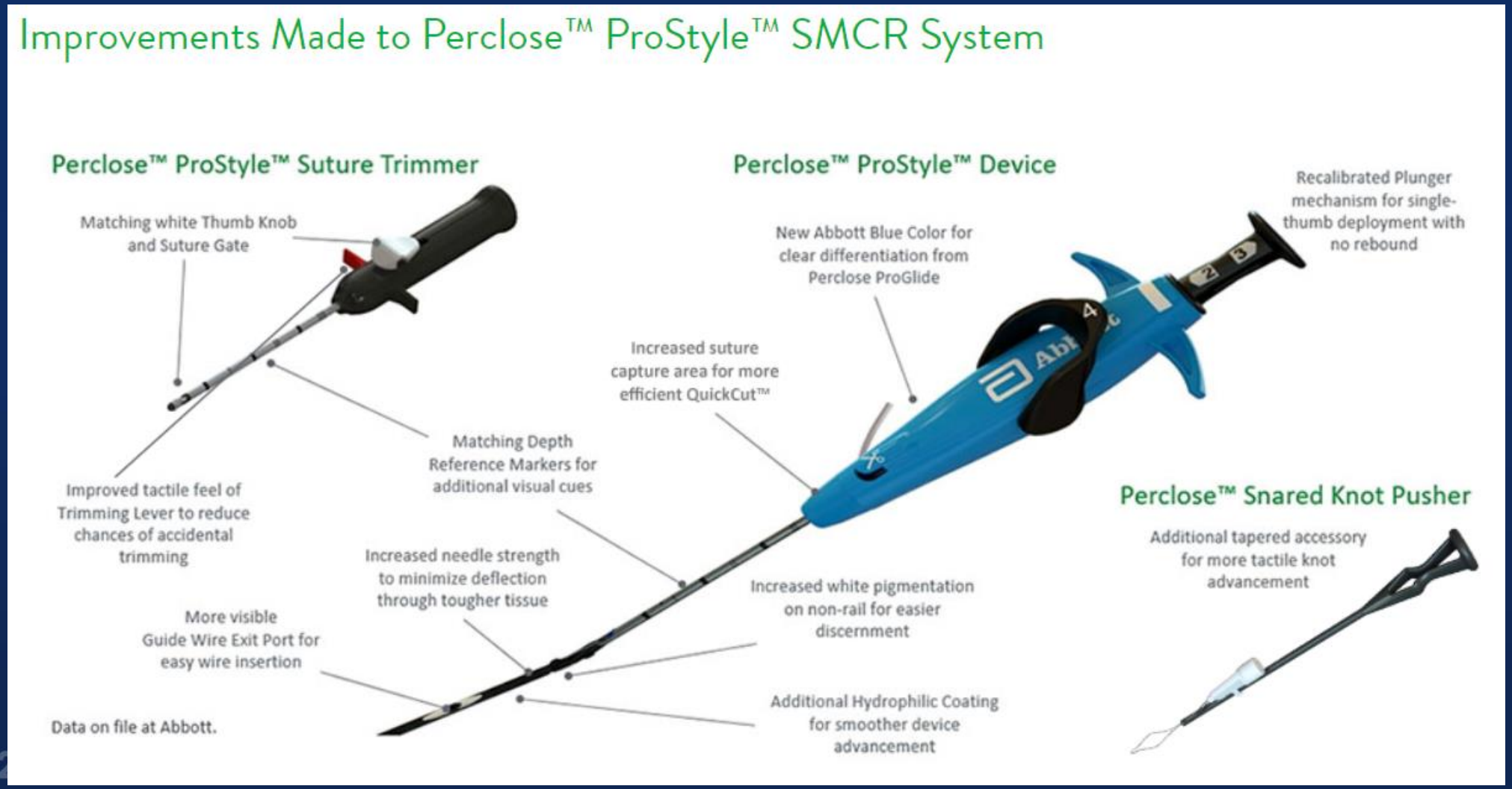
# Perclose ProStyle ®

## Abbott Vascular Devices



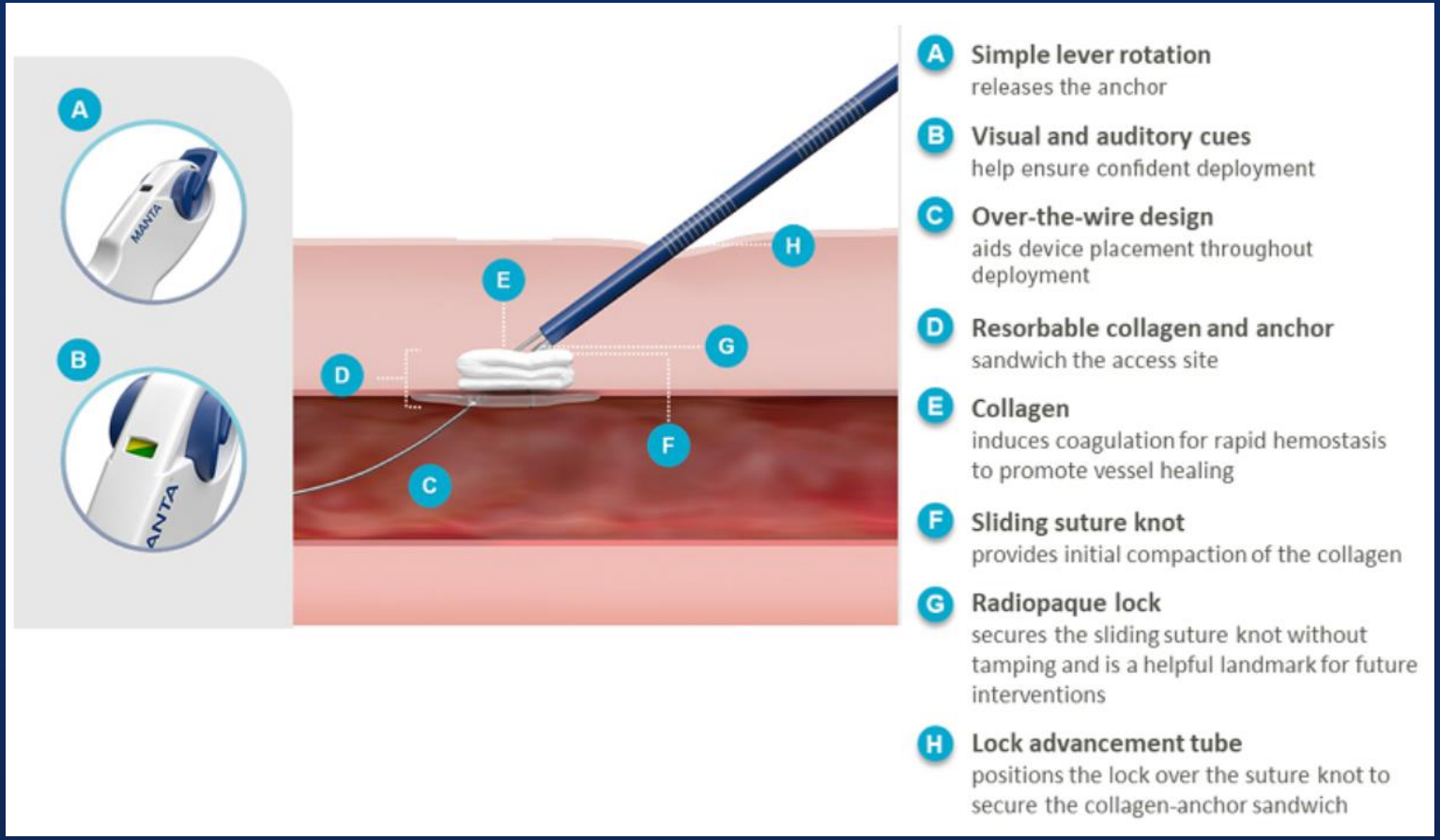
# Perclose ProStyle ®

## Abbott Vascular Devices

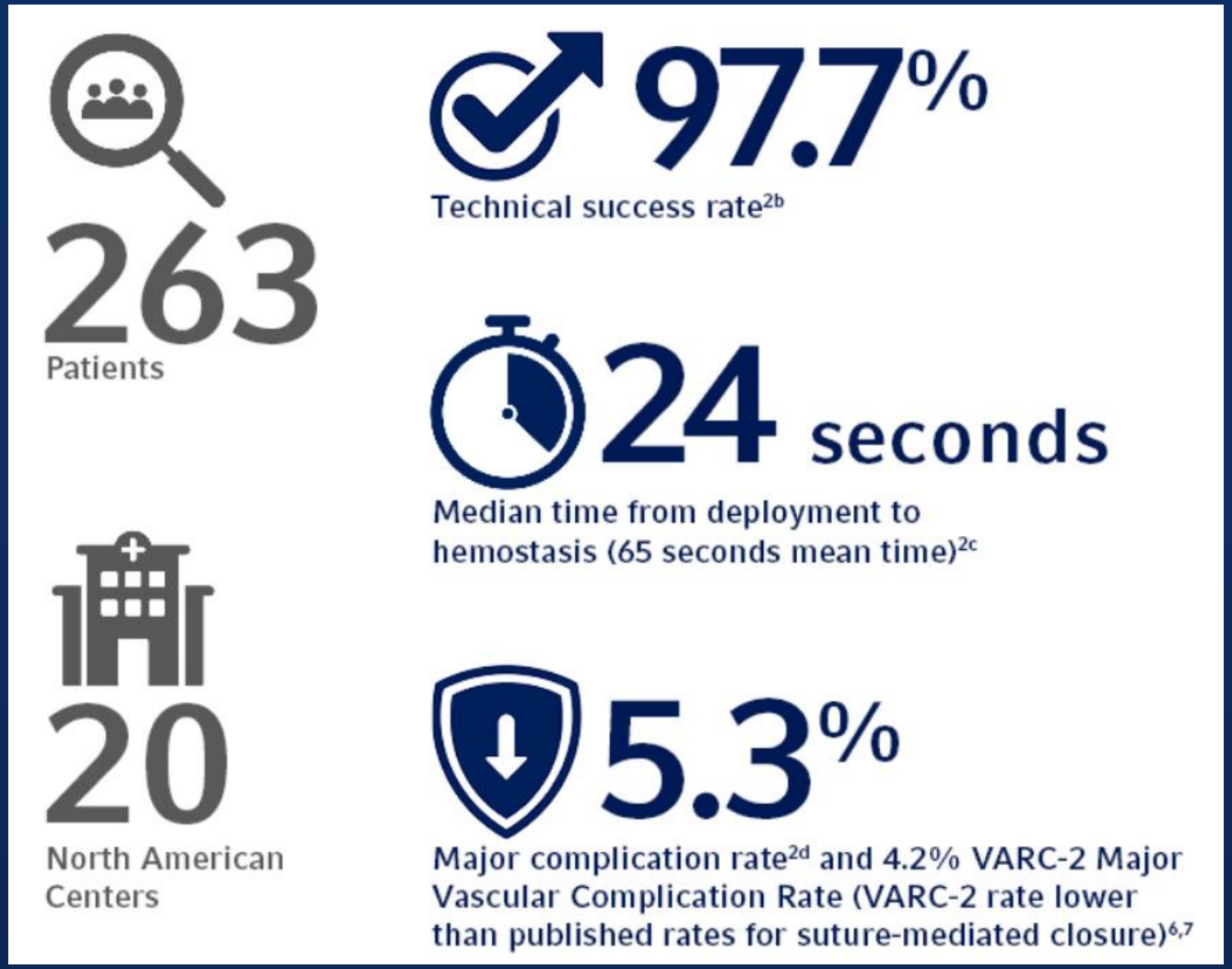


# MANTA Vascular Closure

- 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

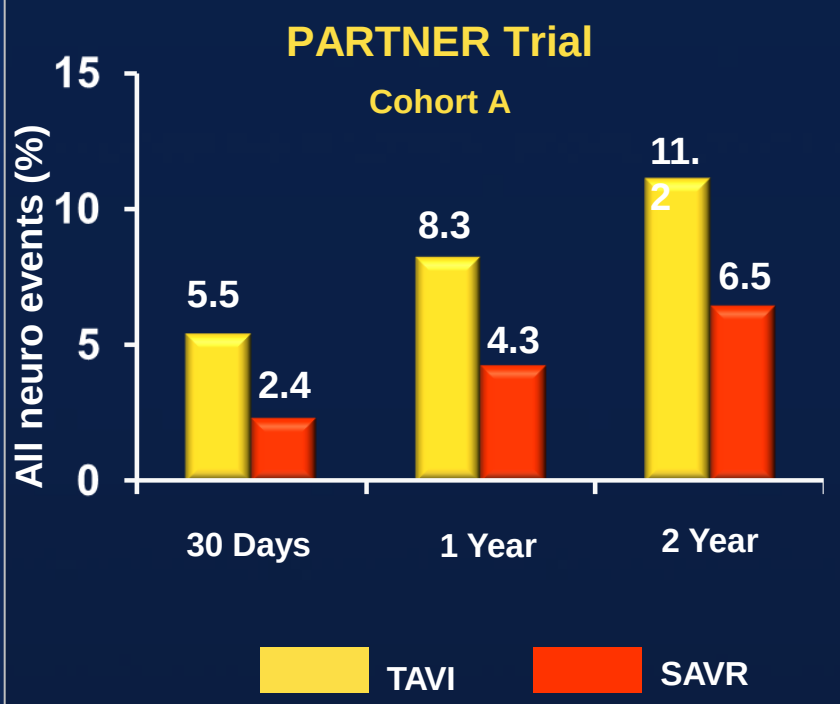
# Complications

# 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

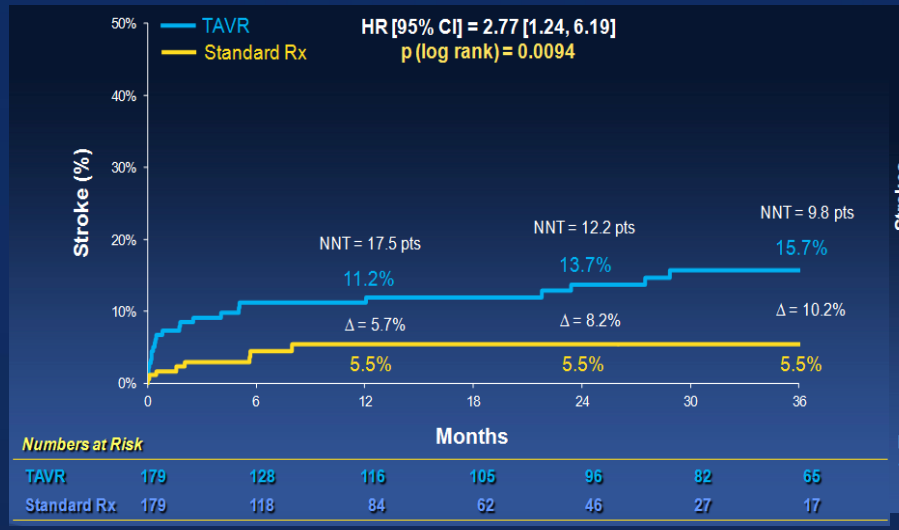
## Incidence of Stroke



# PARTNER trial : All Stroke (ITT)

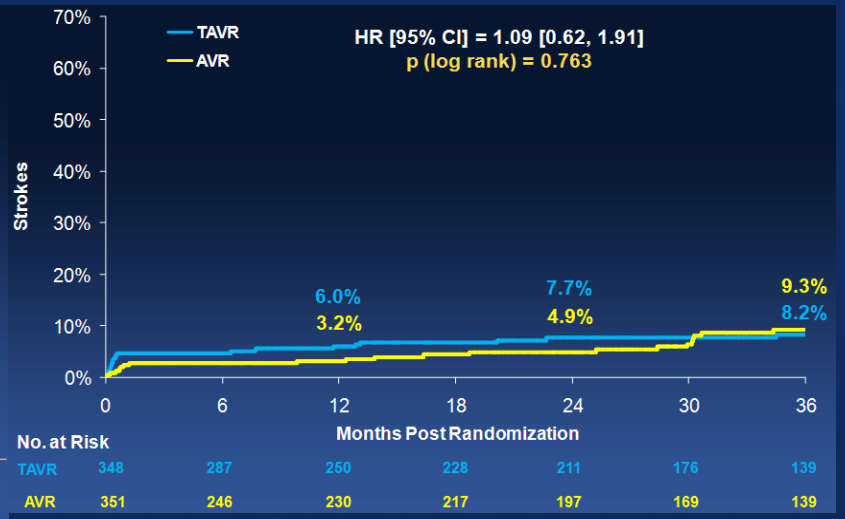
## 3 year follow-up

### Inoperable Cohort




Samir R. Kapadia et al. TCT 2012

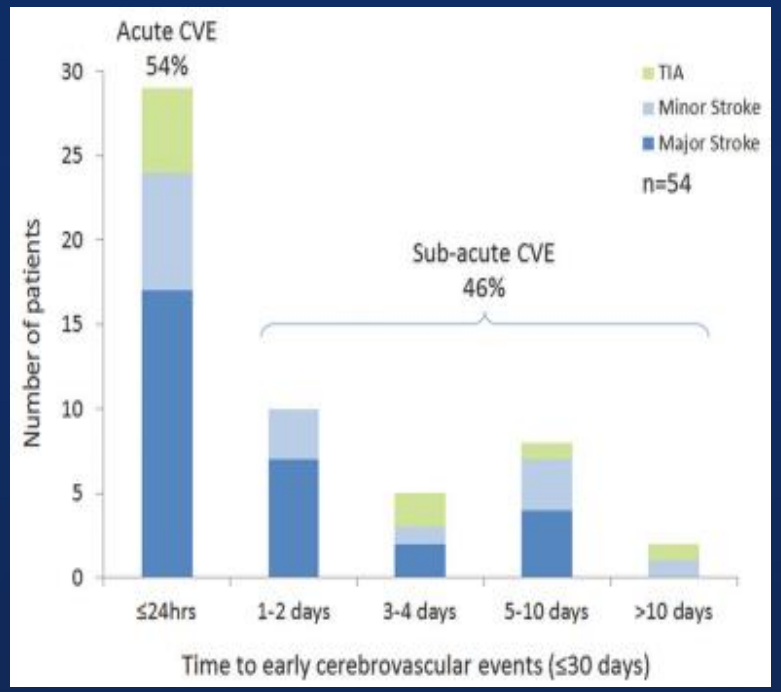
### High Risk Cohort




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.**

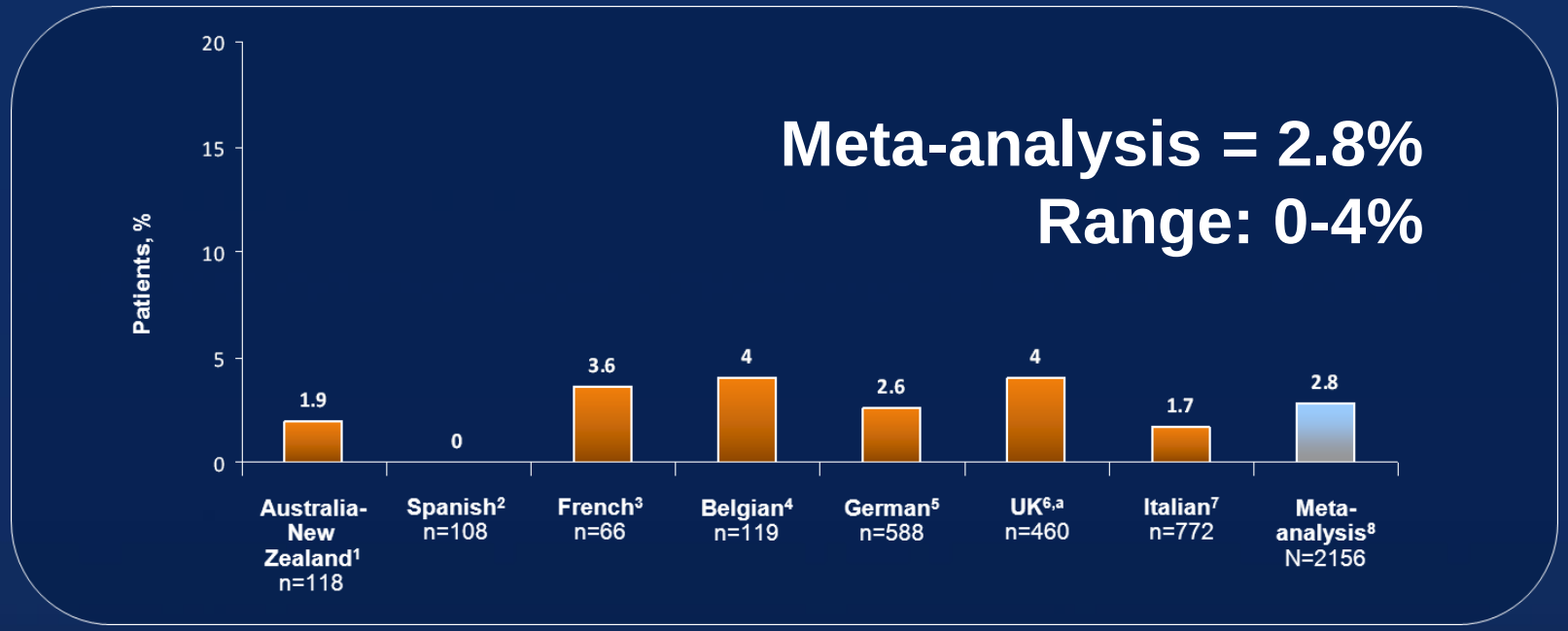



- Acute events (≤24 hrs) independently predicted by balloon postdilation and valve dislodgement/ embolization
- Subacute events (1-30 days) predicted by new onset A-fib, while late events (> 30 days) associated with chronic A-fib, PVD, and cerebrovascular disease
- Major stroke predicts mortality both 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

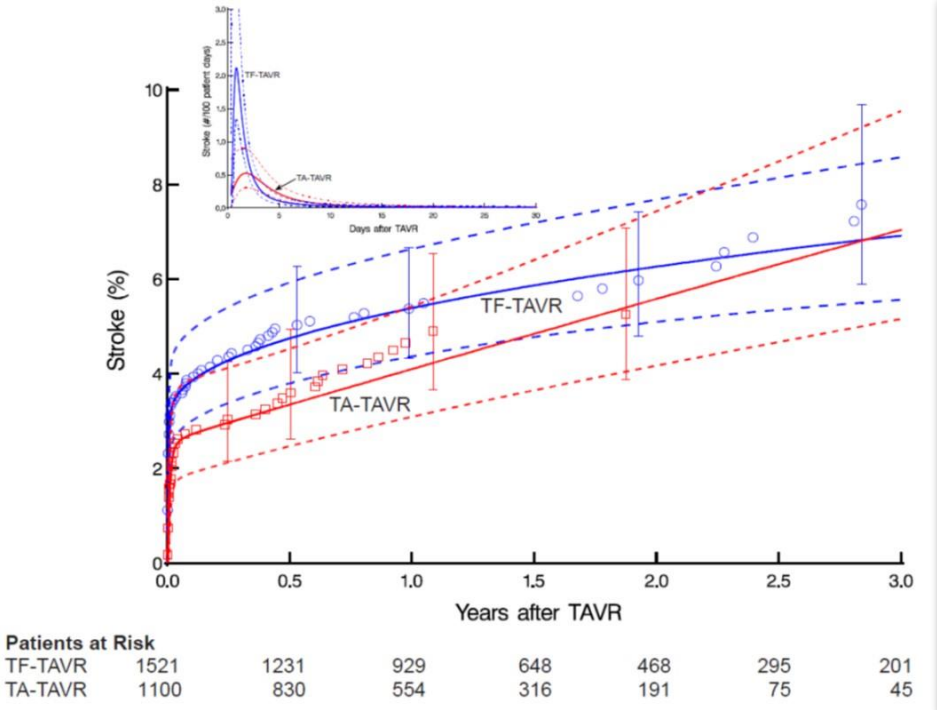



Stroke is not defined consistently across all studies.
[a]In-hospital stroke rate reported.


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

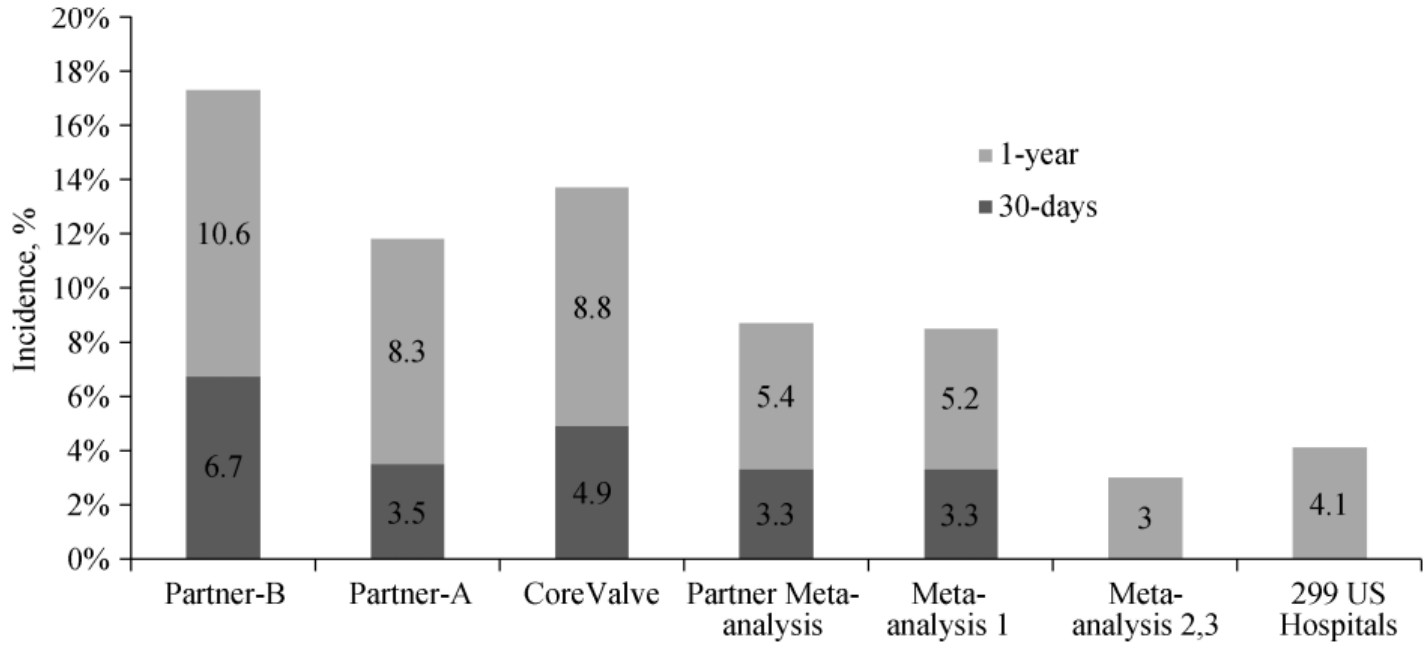
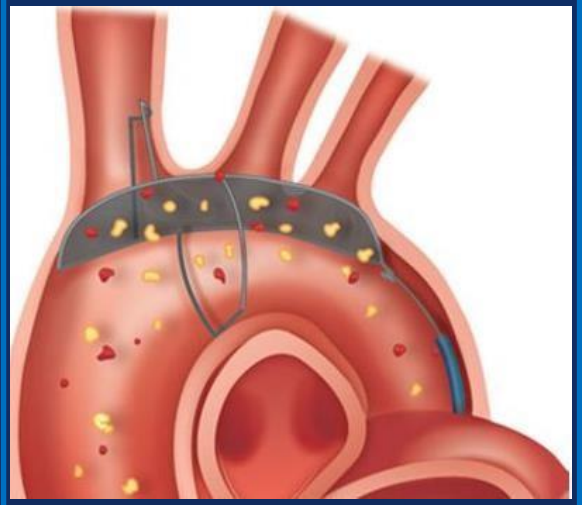



**Figure 1. Incidence of stroke following TAVR in landmark studies and meta-analyses.** PARTNER-B,[4] PARTNER-A,[12] CoreValve,[7] PARTNER Meta-analysis,[11] meta-analysis 1,[15] meta-analyses 2,3,[9,23] and 299 US hospitals.[24] TAVR: transcatheter aortic valve replacement.

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

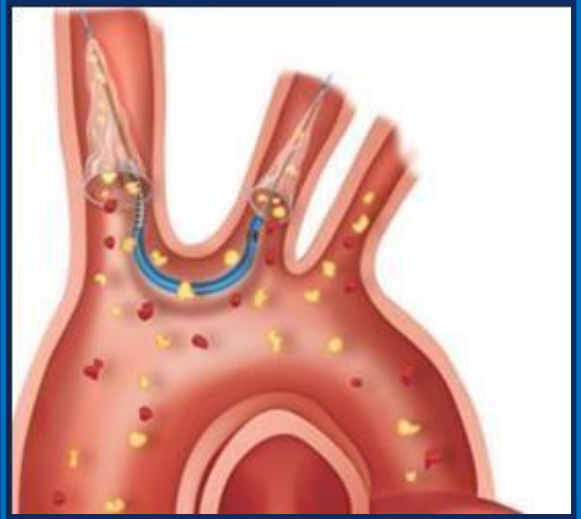
# Embolic protection devices

## TriGuard Embolic Deflection Device (Keystone Heart)[1]



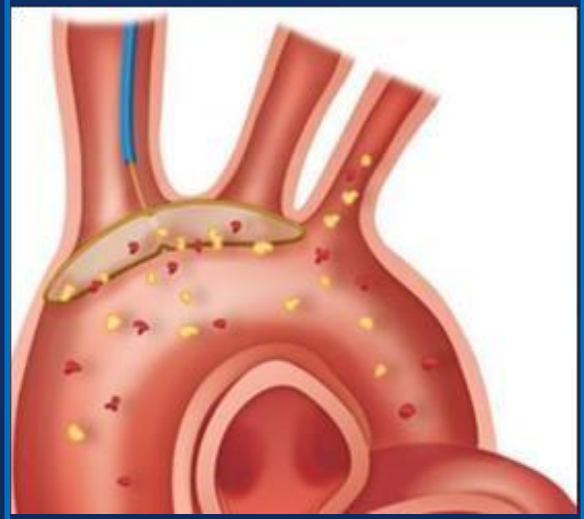
- ✓ Pore Size: 130 µm
- ✓ Delivery Sheath: 9F
- ✓ Access: Transfemoral
- ✓ Coverage: Brachiocephalic, left common carotid, left subclavian

## 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]

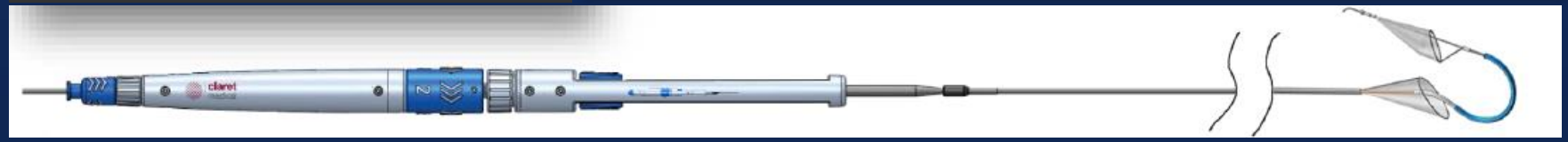


- ✓ Pore Size: 100 µm
- ✓ Delivery Sheath: 6F
- ✓ Access: Brachial
- ✓ Coverage: Brachiocephalic, left common carotid

[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

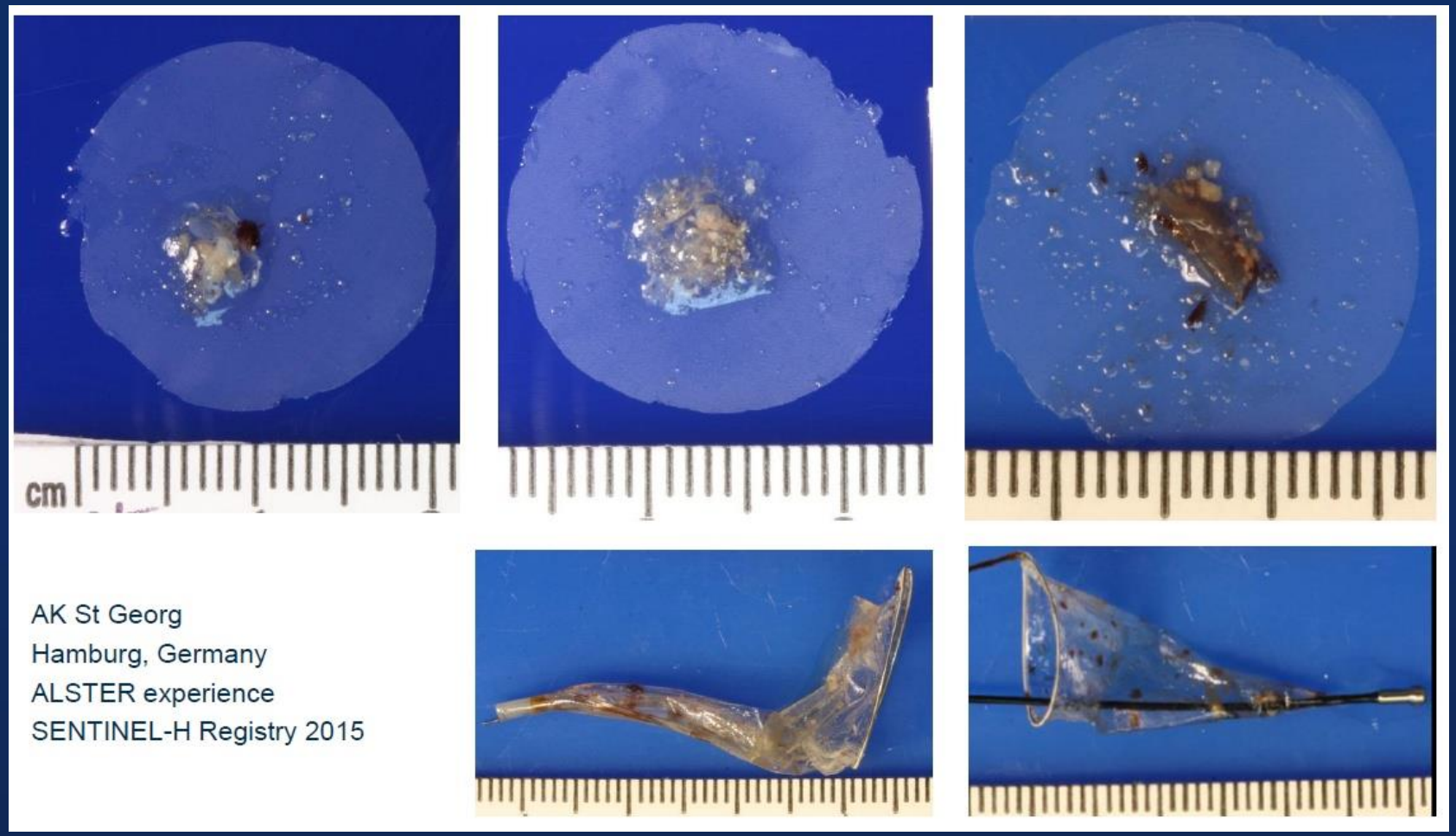
# Claret Sentinel™ Cerebral Protection System (CPS)

- 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

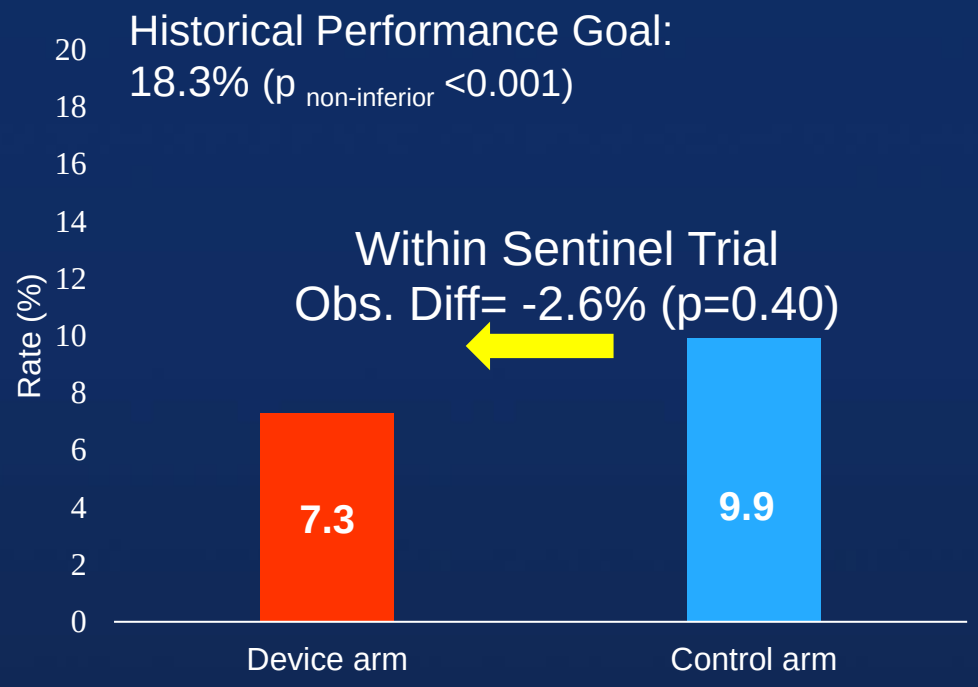



Susheel Kodali, TCT 2015

# SENTINEL Trial

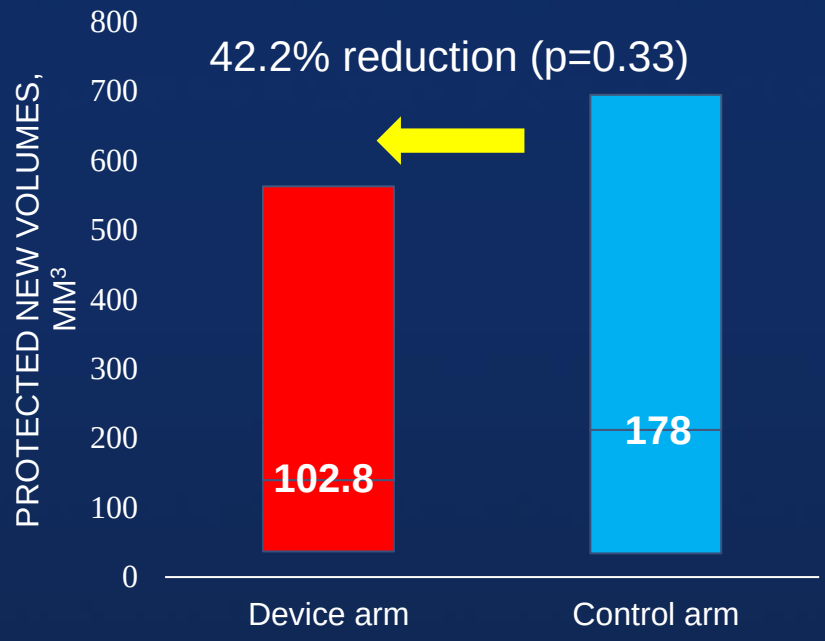
## Primary Safety Endpoint

*30-Day MACCE*




## Primary Efficacy Endpoint

*MRI New Lesion Volume (Protected Territories)*




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

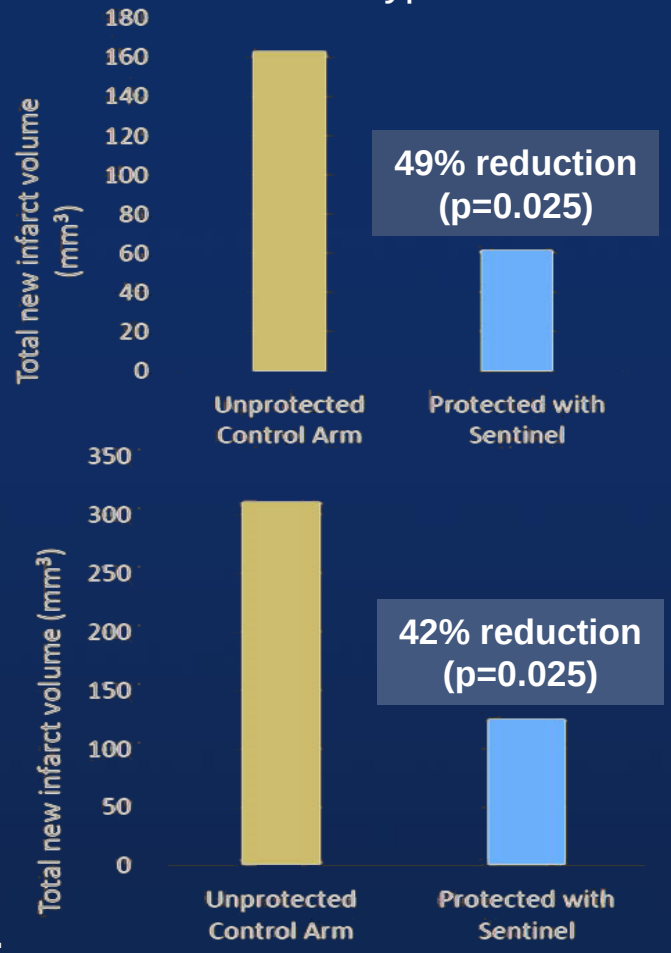
# SENTINEL Trial

## 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

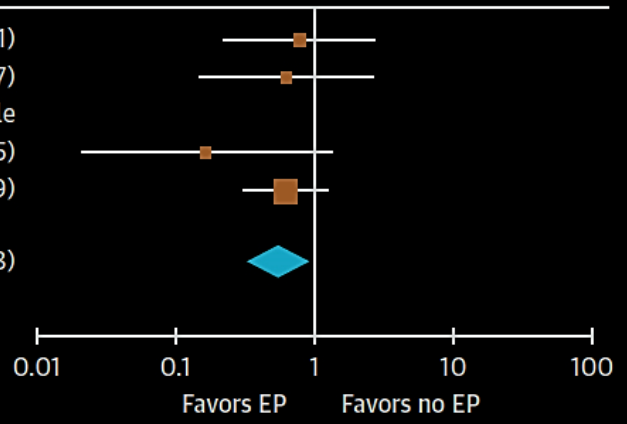
**FIGURE 1** Clinical Outcomes in Patients Undergoing TAVR With Versus Without Embolic Protection Devices

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: $Z = 2.01$ ($P = 0.04$)

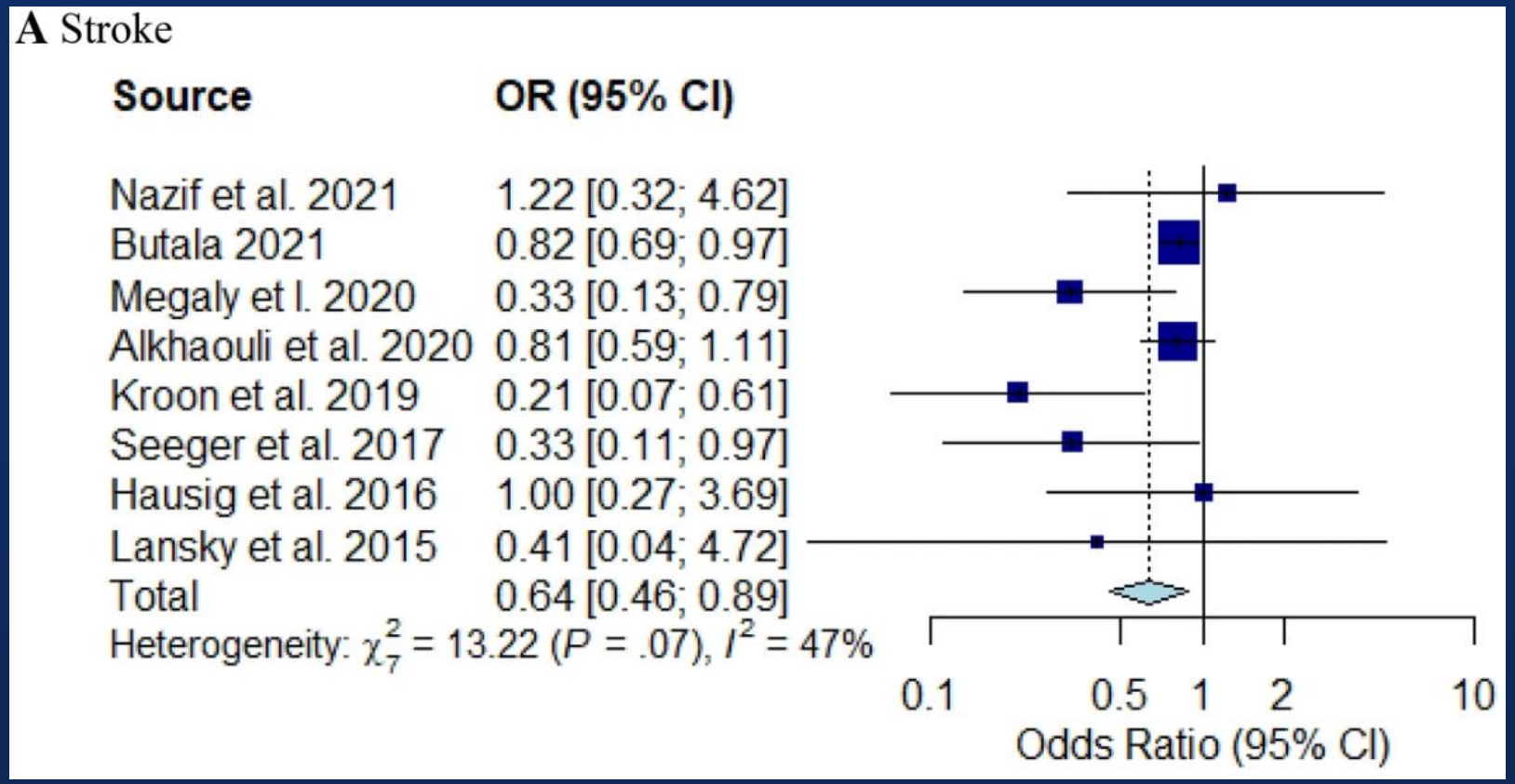



Pooled effect estimates for the risk of death or stroke according to the use of cerebral embolic protection versus not during TAVR. CI = confidence interval; CLEAN-TAVI = Claret Embolic Protection and TAVI; DEFLECT-III = A Prospective, Randomized Evaluation of the TriGuard HDH Embolic Deflection Device 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

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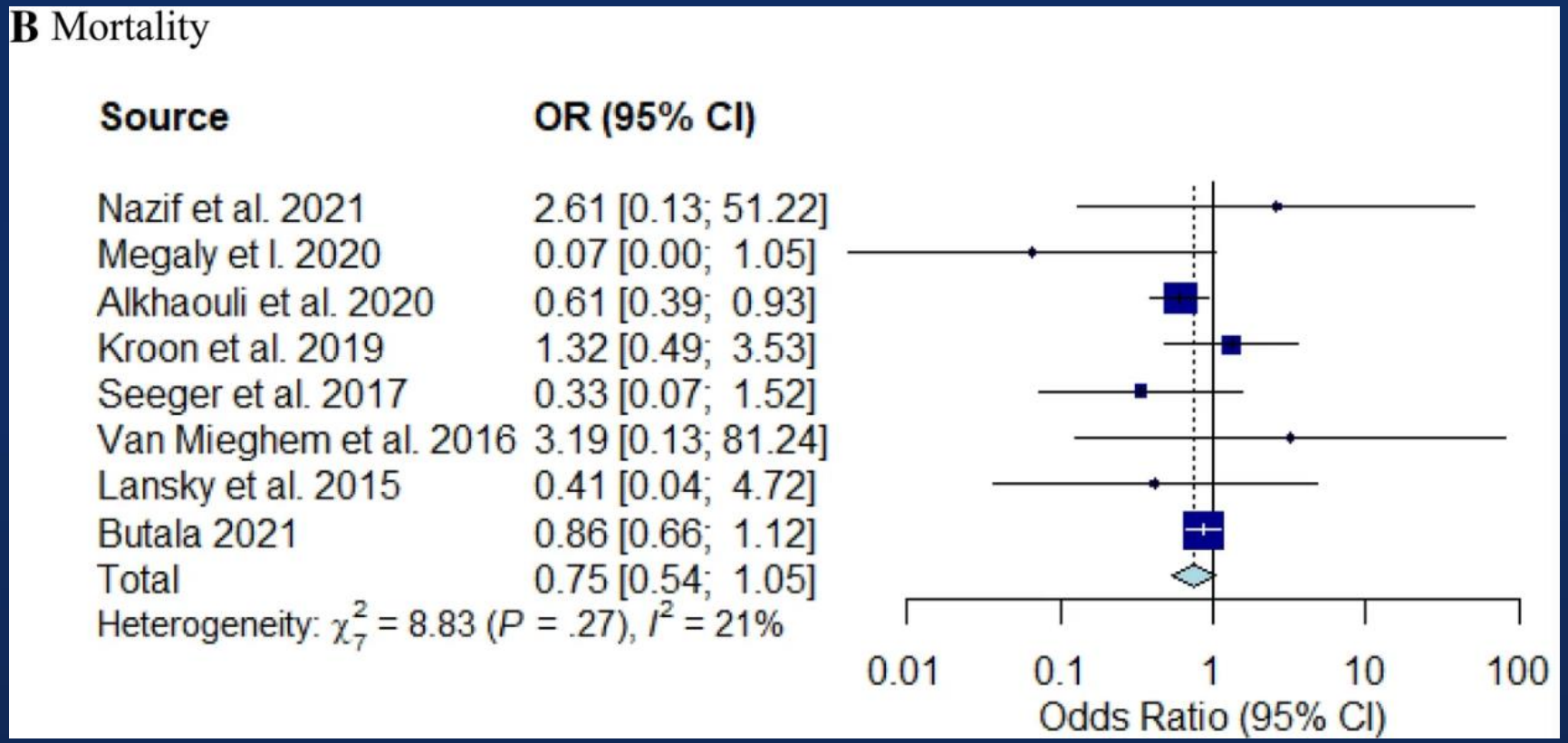


Junichi Shimamura et al. Cardiovasc Interv Ther. 2022;37(3):549-557

# Safety and efficacy of Cerebral Embolic Protection device undergoing TAVR

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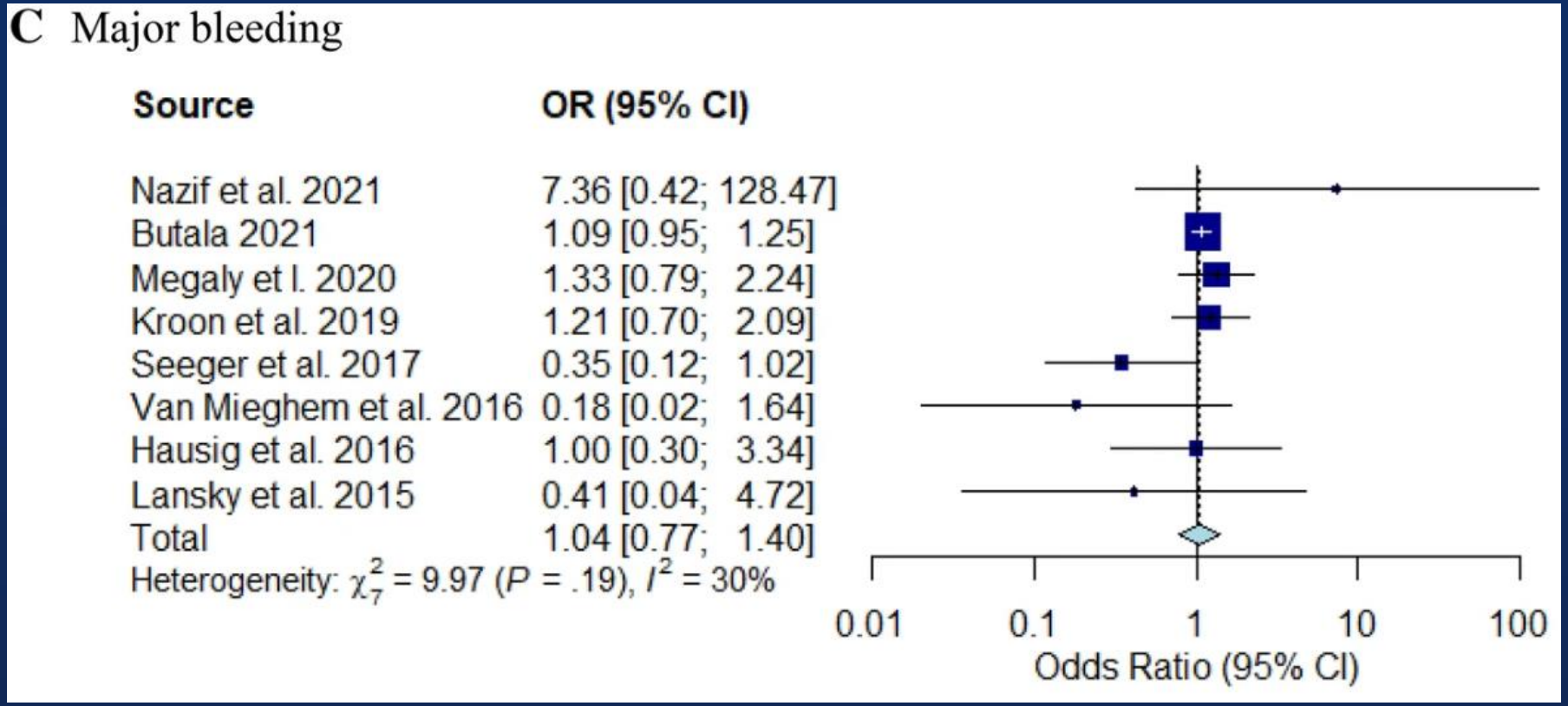
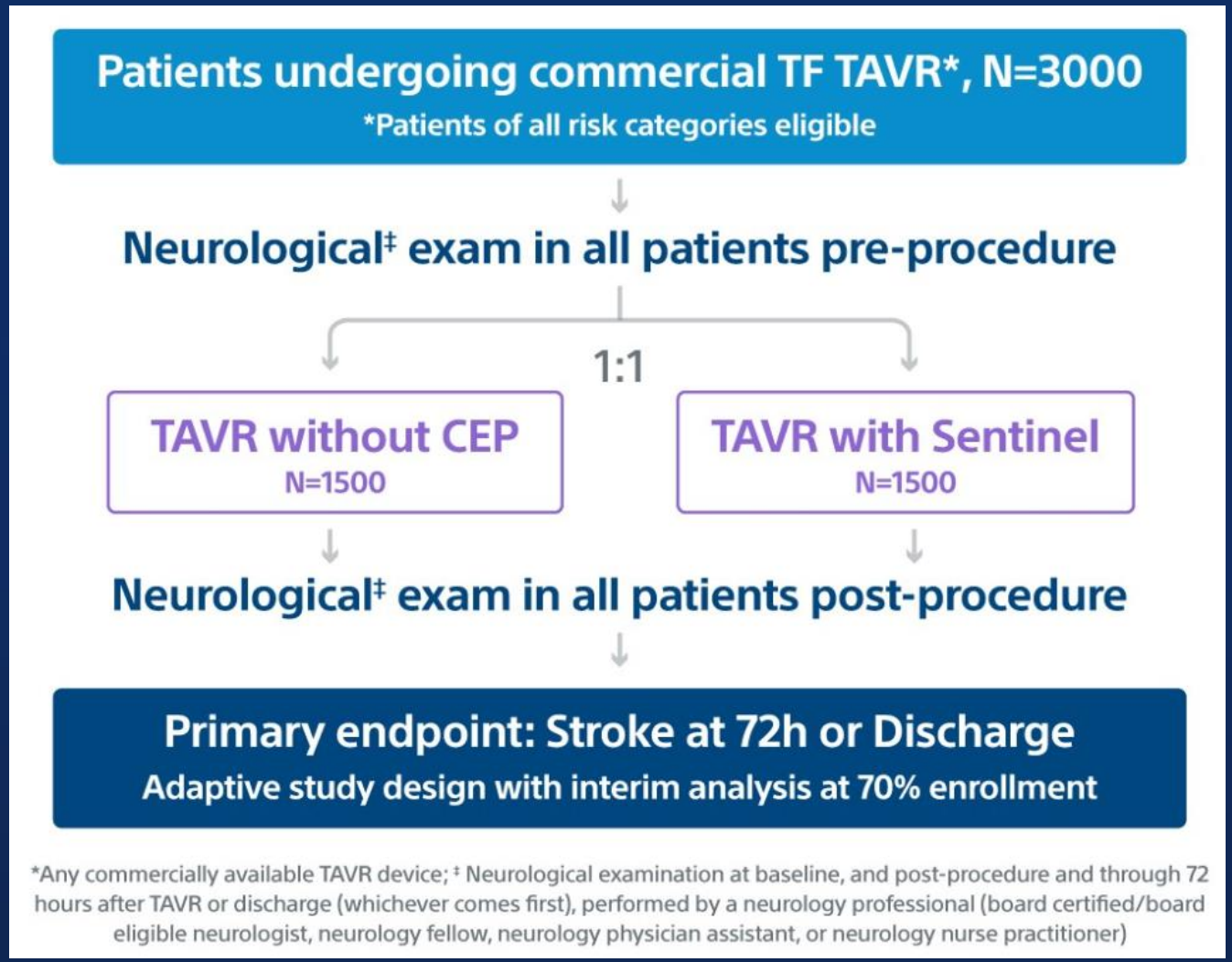
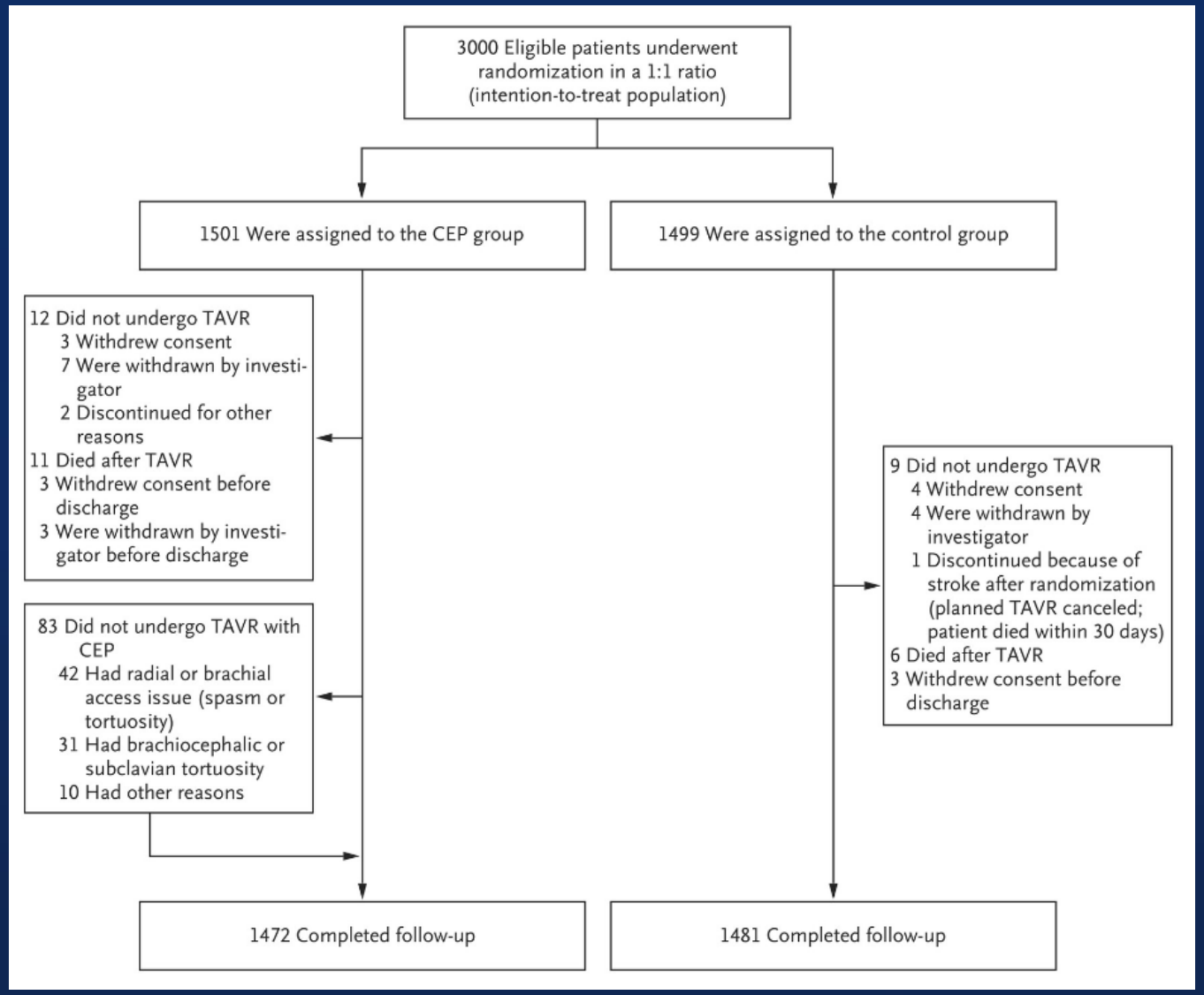



Junichi Shimamura et al. Cardiovasc Interv Ther. 2022;37(3):549-557

# PROTECTED TAVR Trial



# PROTECTED TAVR Trial



# PROTECTED TAVR Trial

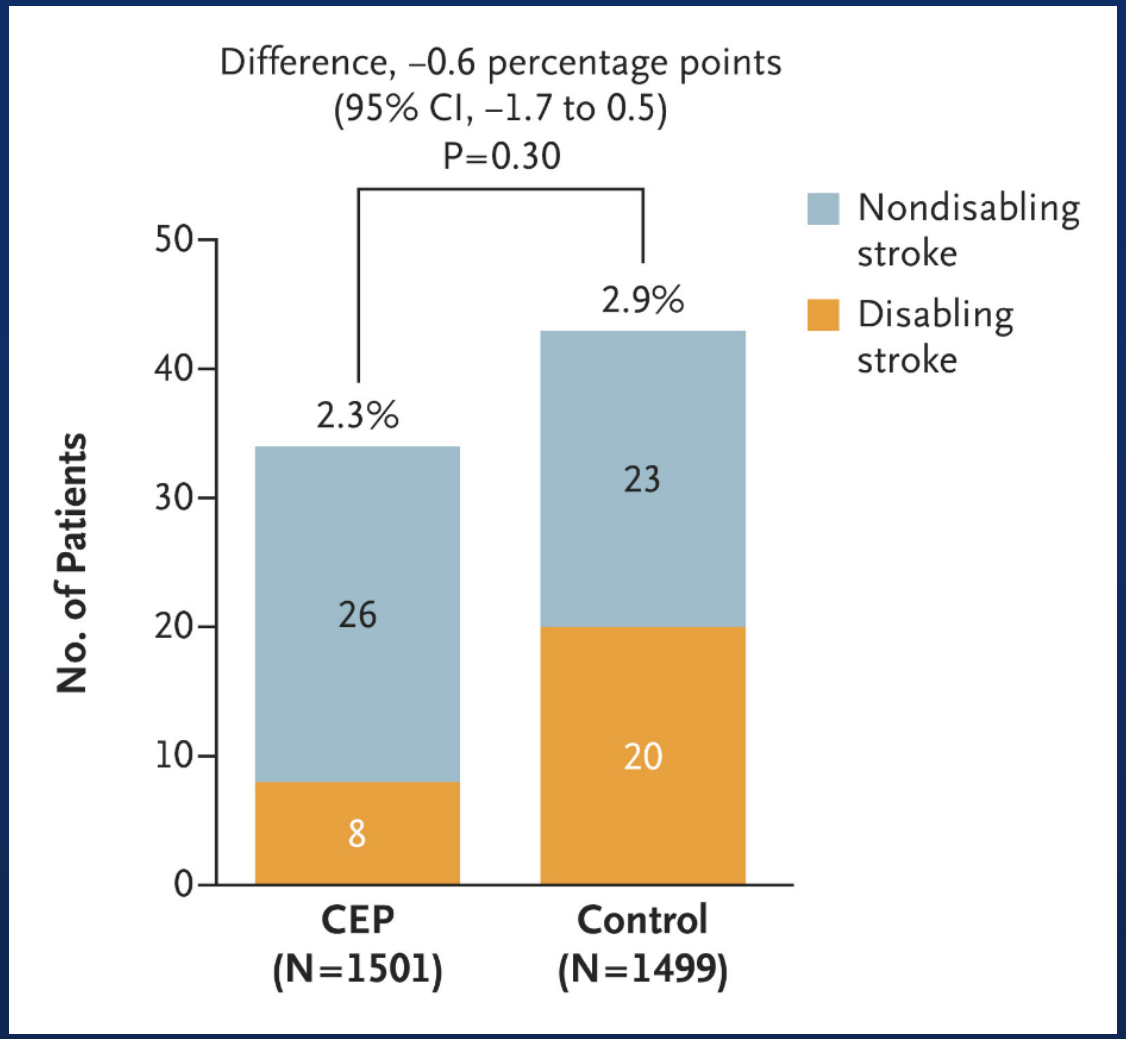



**Table 2.** Clinical and Neurologic Outcomes within 72 Hours after TAVR or before Discharge.*

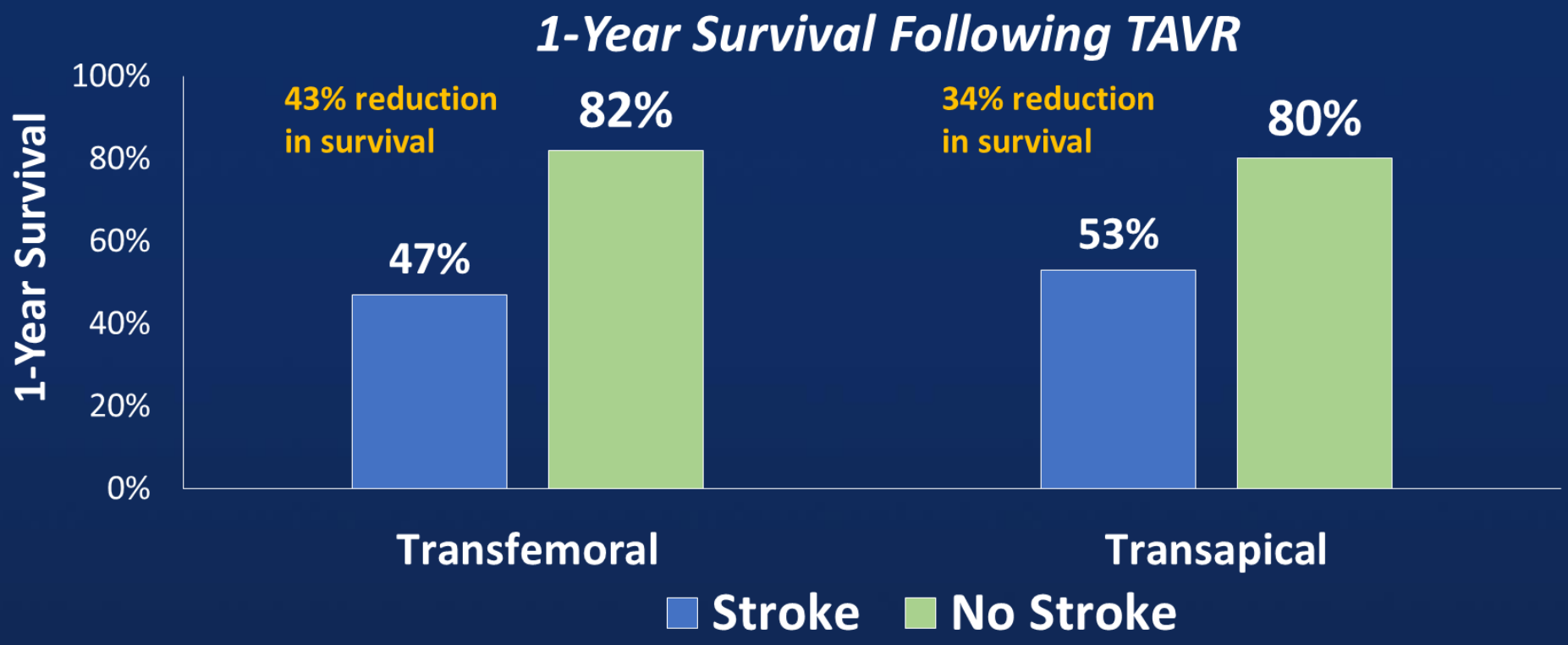
| Outcome | CEP (N=1501) | Control (N=1499) | Difference (95% CI)† |
|---|---|---|---|
| **Clinical** | | | |
| Primary end point: stroke — no. (%) | 34 (2.3) | 43 (2.9) | –0.6 (–1.7 to 0.5) |
| Disabling | 8 (0.5) | 20 (1.3) | –0.8 (–1.5 to –0.1) |
| Ischemic | 6 (0.4) | 17 (1.1) | –0.7 (–1.4 to –0.1) |
| 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

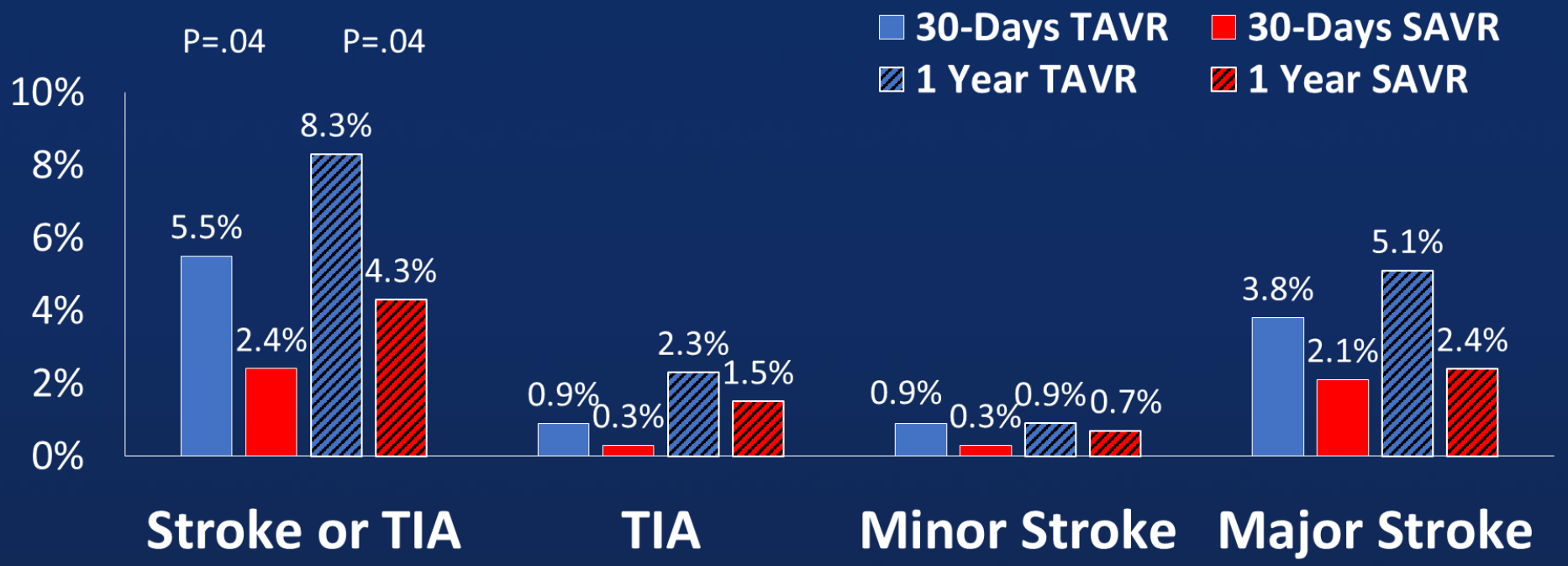
Samir R. Kapadia et al, J Am Coll Cardiol. 2018;72:2415–26.

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



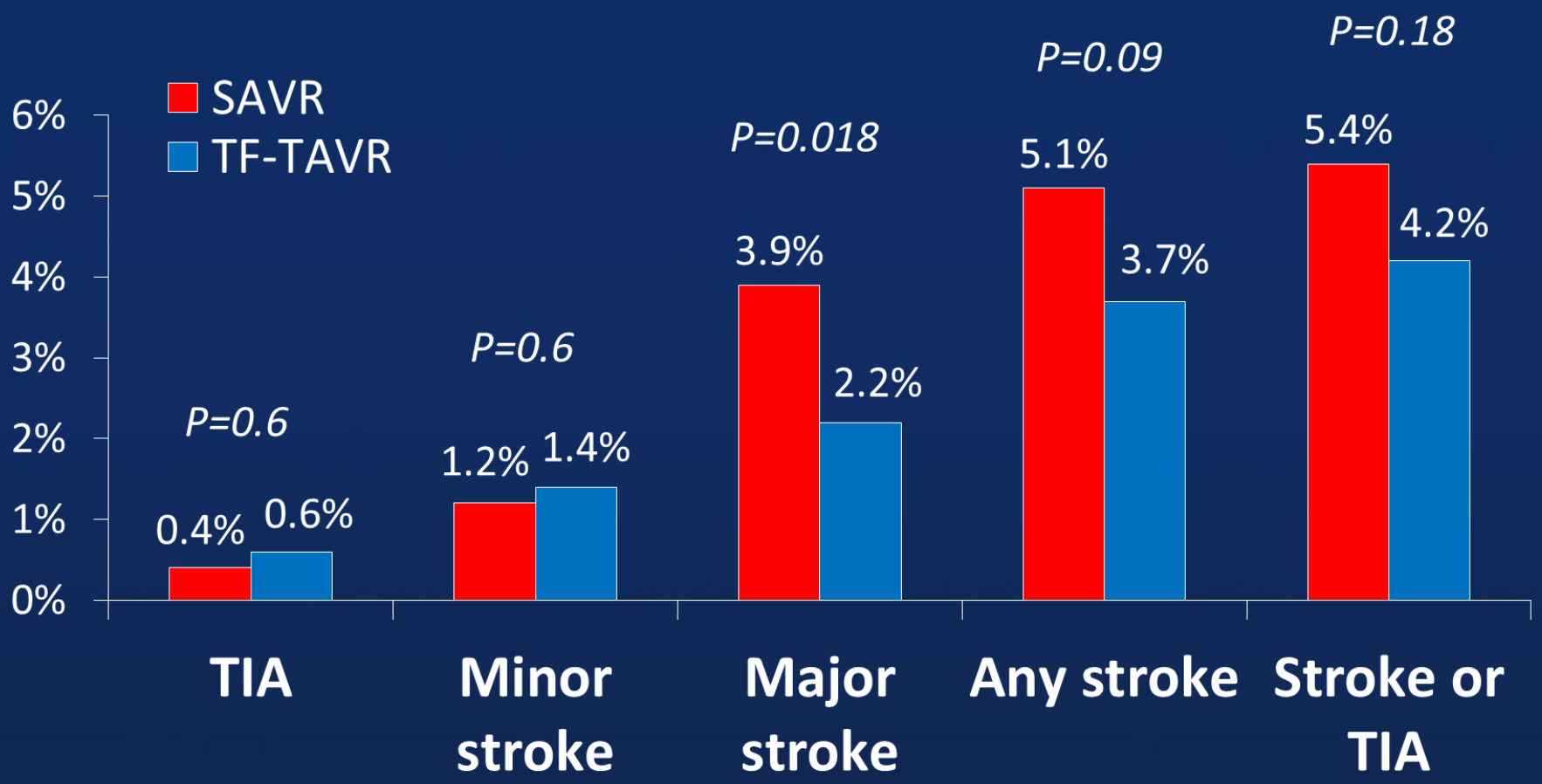

Kapadia et al. Circ Cardiovasc Interv. 2016

# PARTNER 1A Raised Concern of Increased Neurologic Risk of TAVR



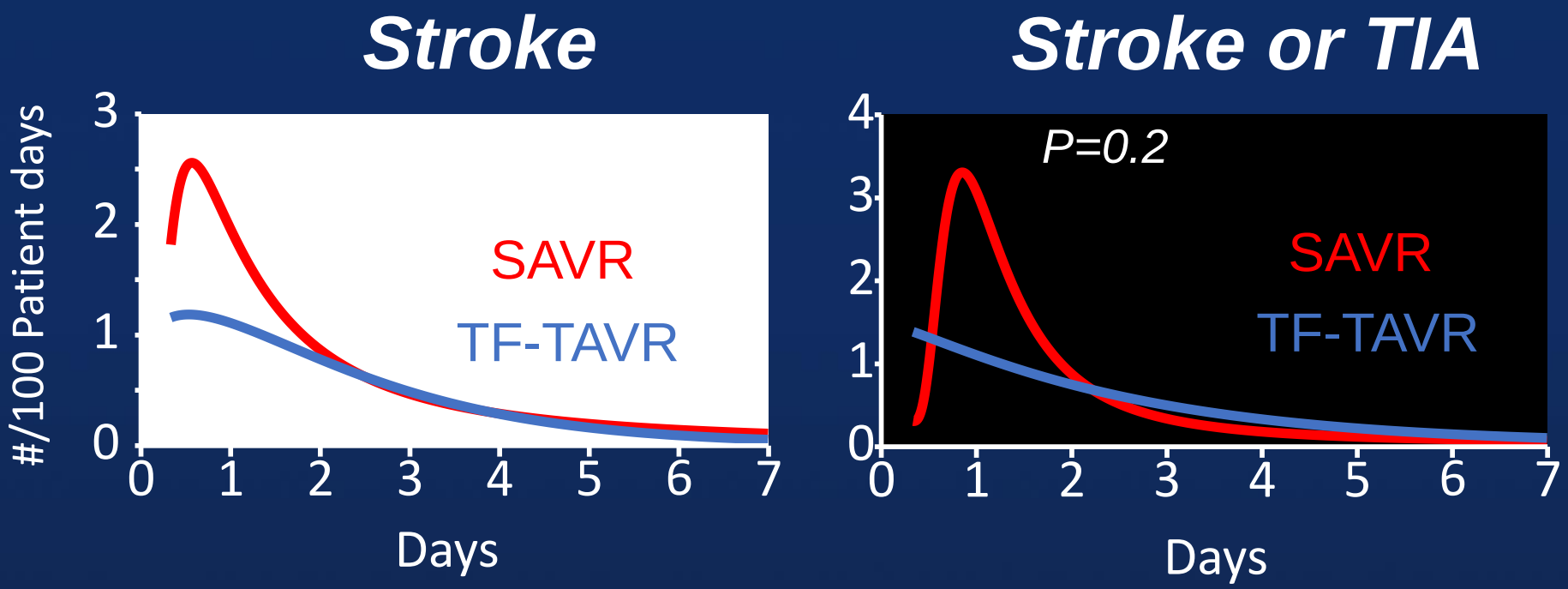

Smith et al. N Engl J Med. 2011; 364:2187-98

# SAVR vs. TF-TAVR
## 30-Day Neurologic Events



# Early Phase Risk (<7 Days)

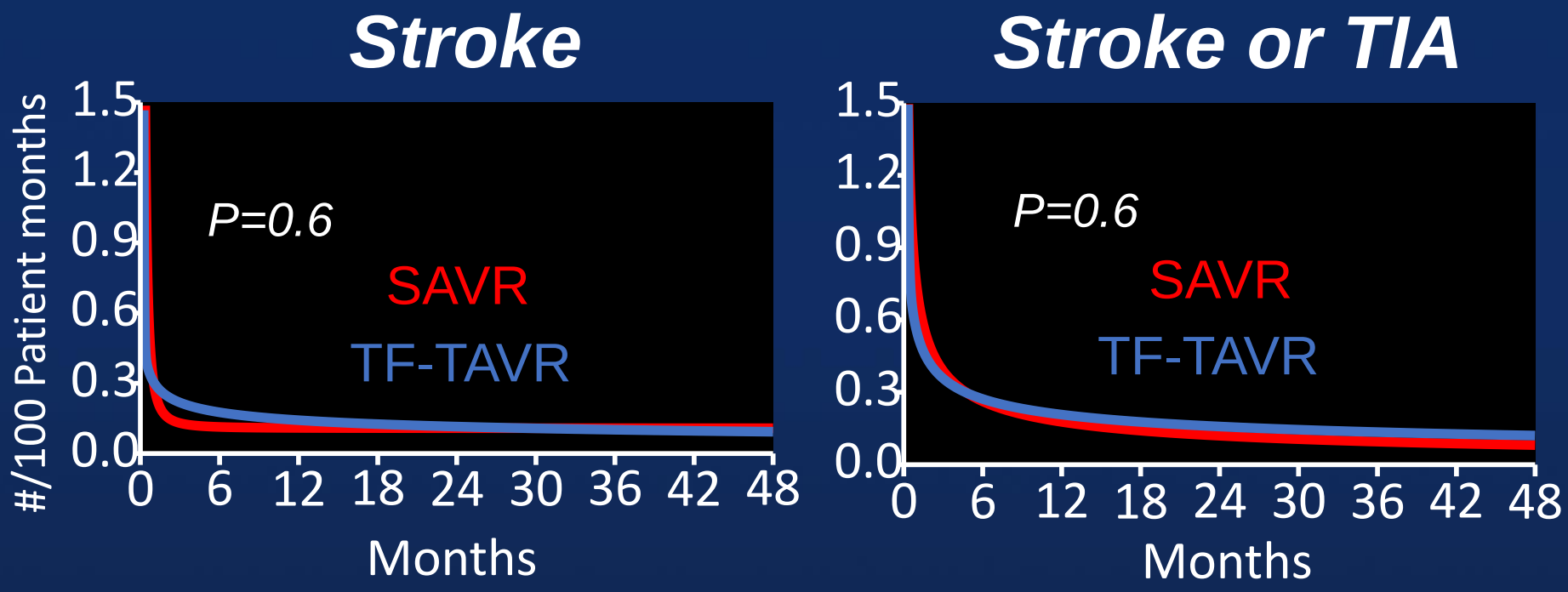
*Instantaneous Risk Modeling*




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

# Late Phase Risk (4 Years)

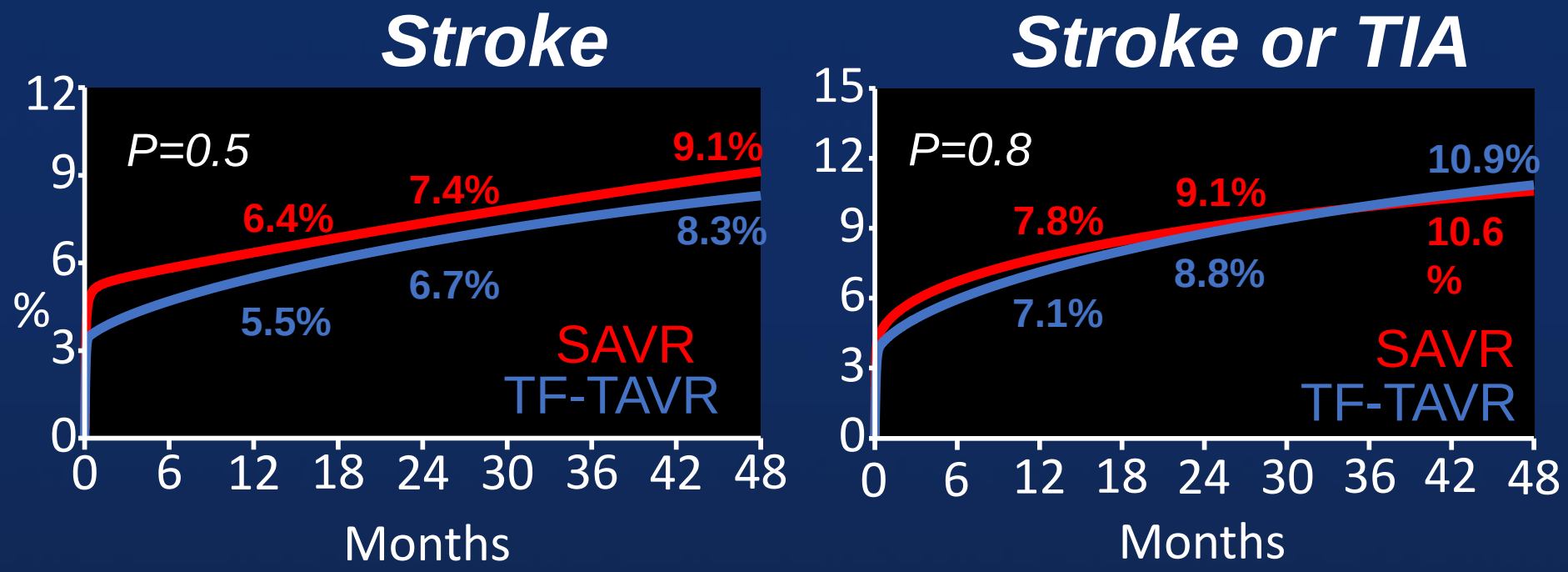
***Instantaneous Risk Modeling***




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

# Cumulative Incidence of Events

***Adjusted for Competing Risk of Mortality***



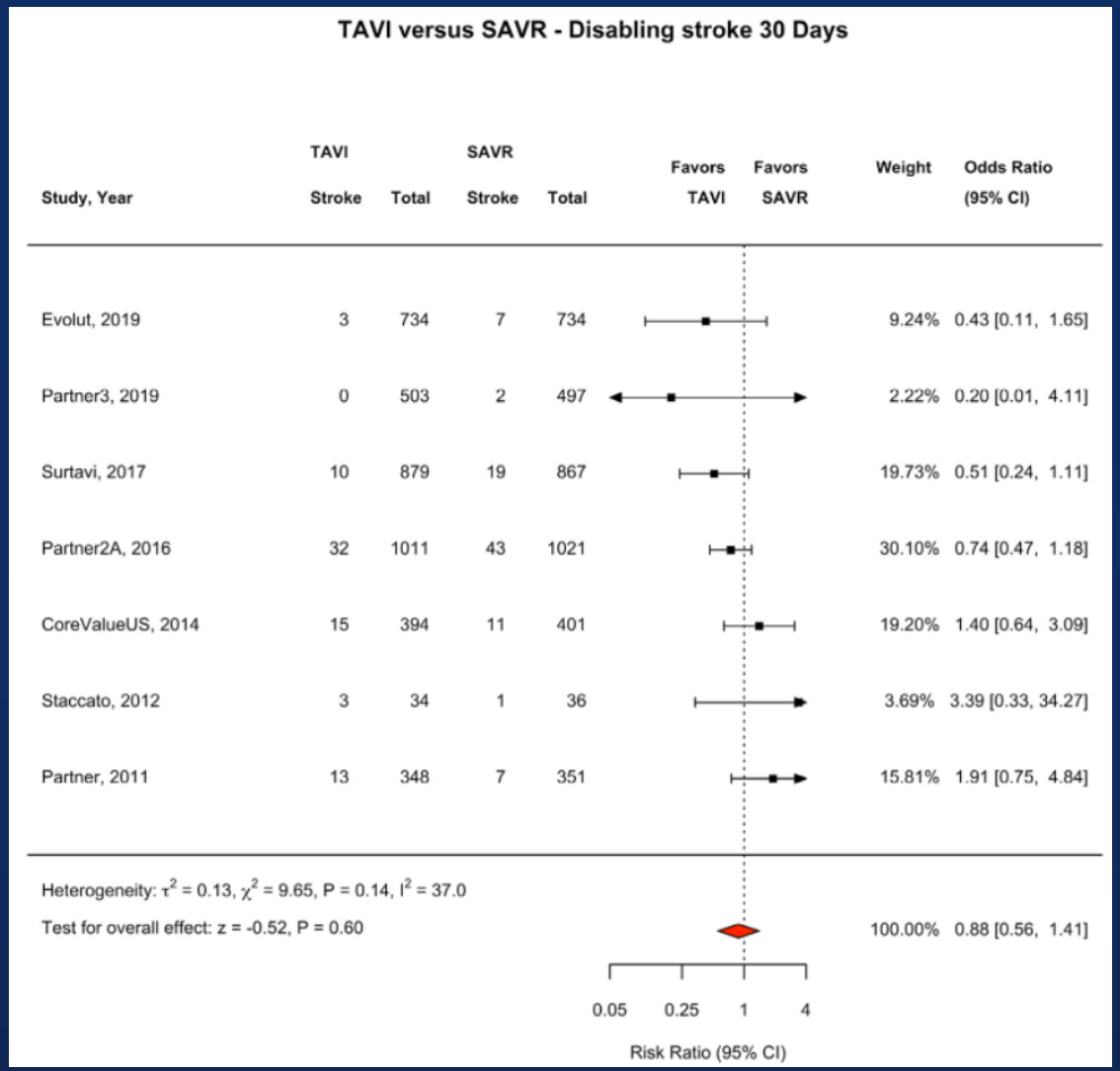

Samir R. Kapadia et al, J Am Coll Cardiol. 2018;72:2415–26.

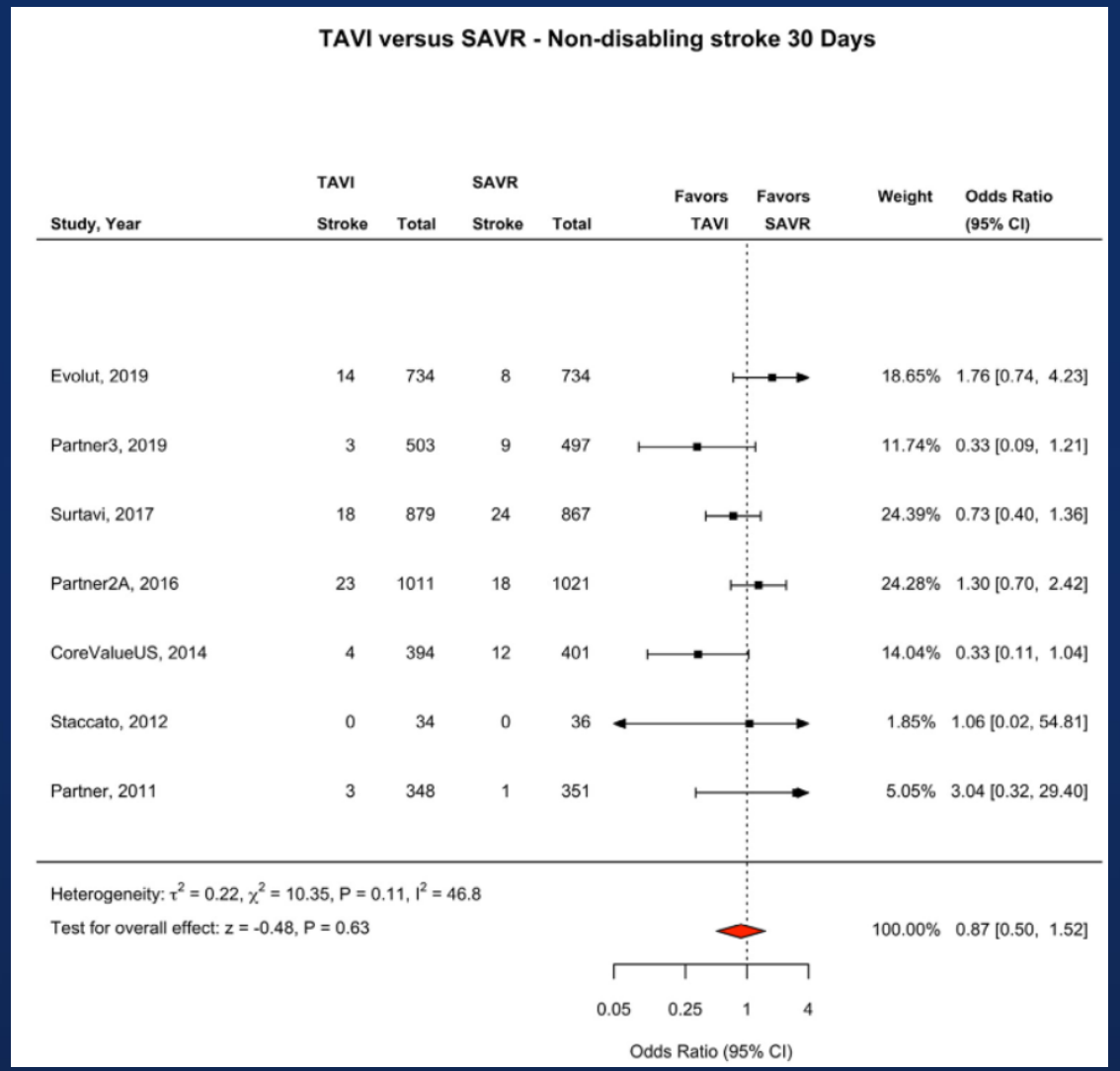
# Stroke Severity in TAVR vs SAVR

## : 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

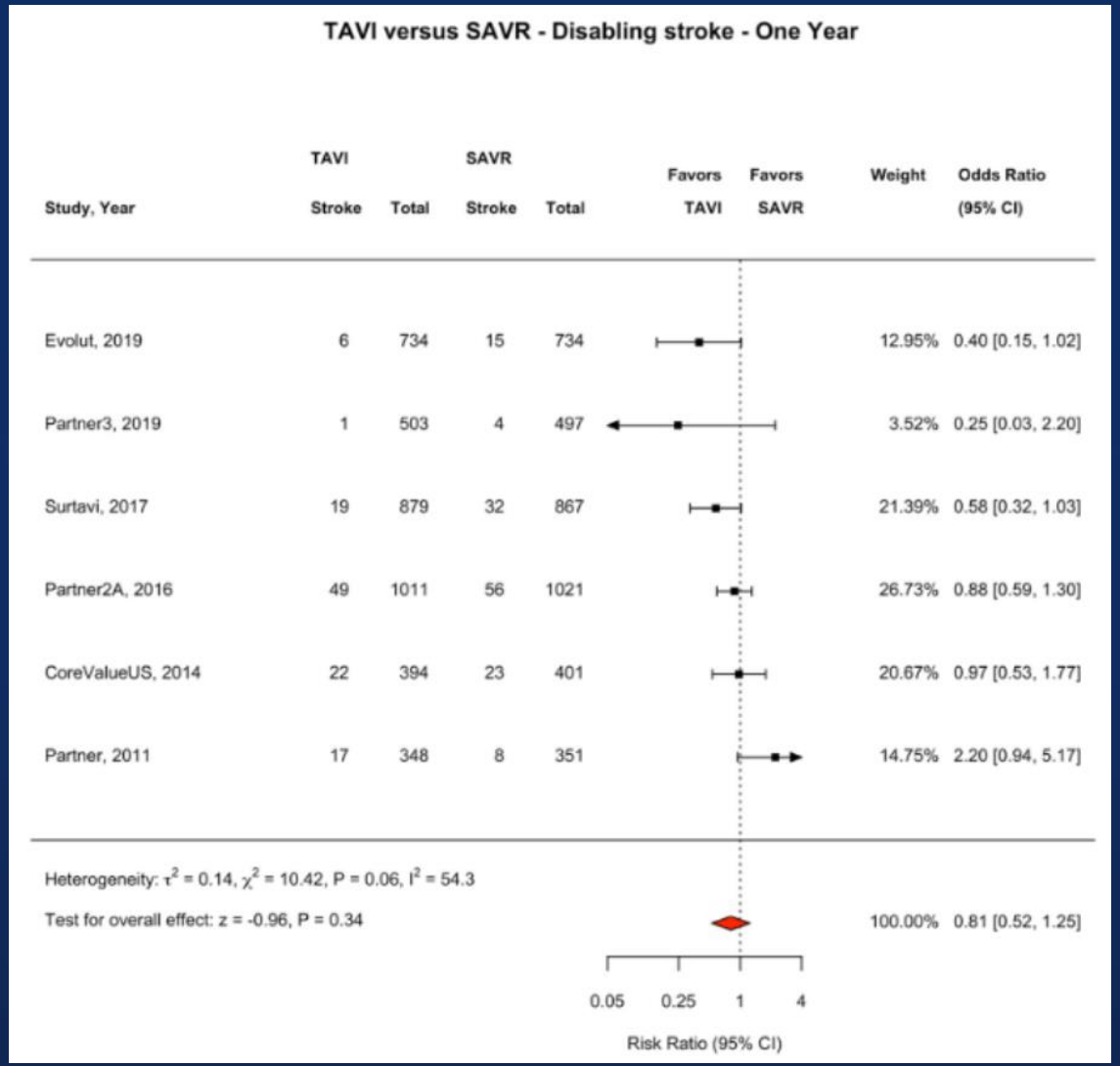


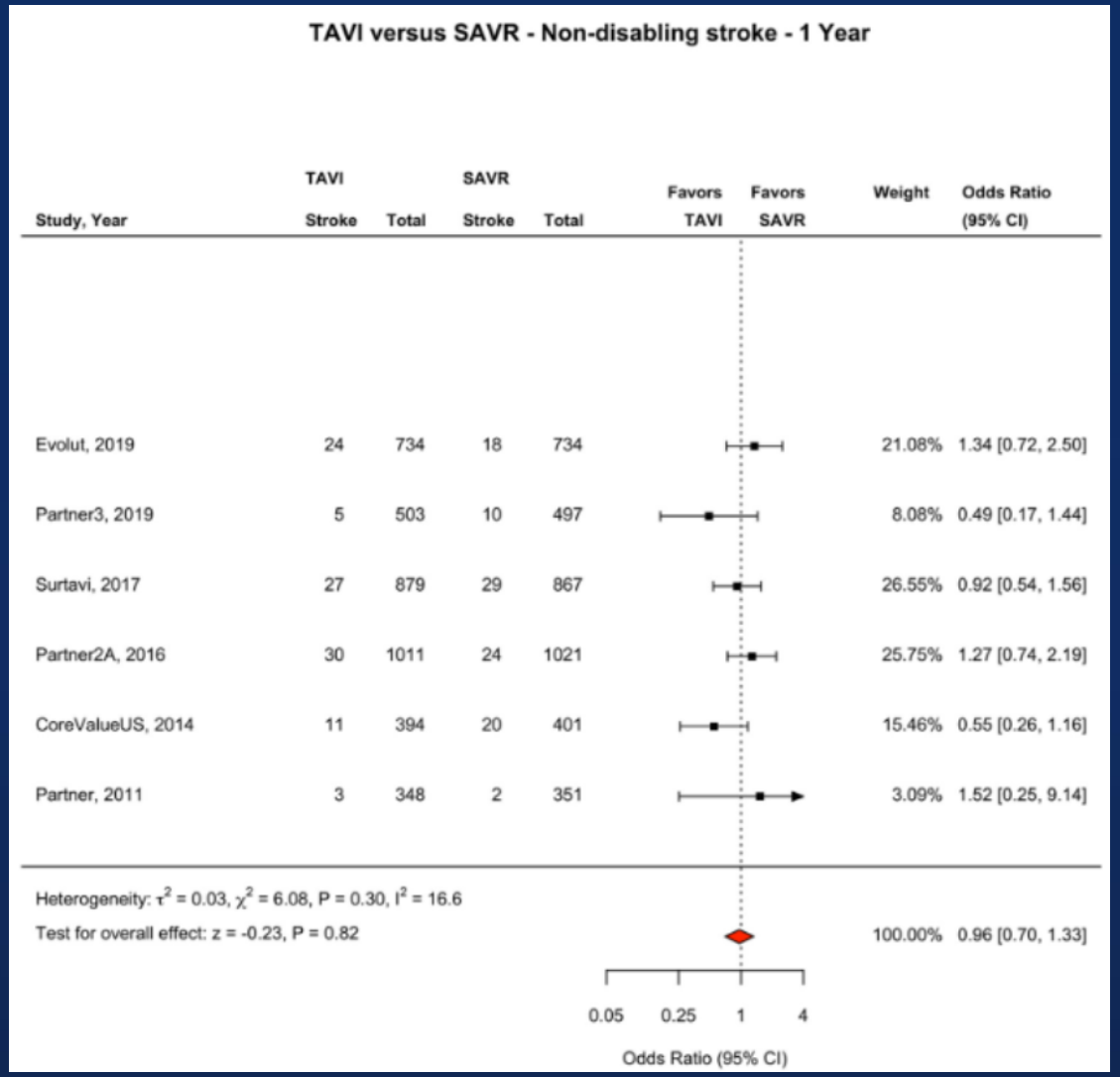






Padraig Synnott MB et al, Journal of Stroke and Cerebrovascular Diseases, Vol. 30, No. 9 (September), 2021:105927

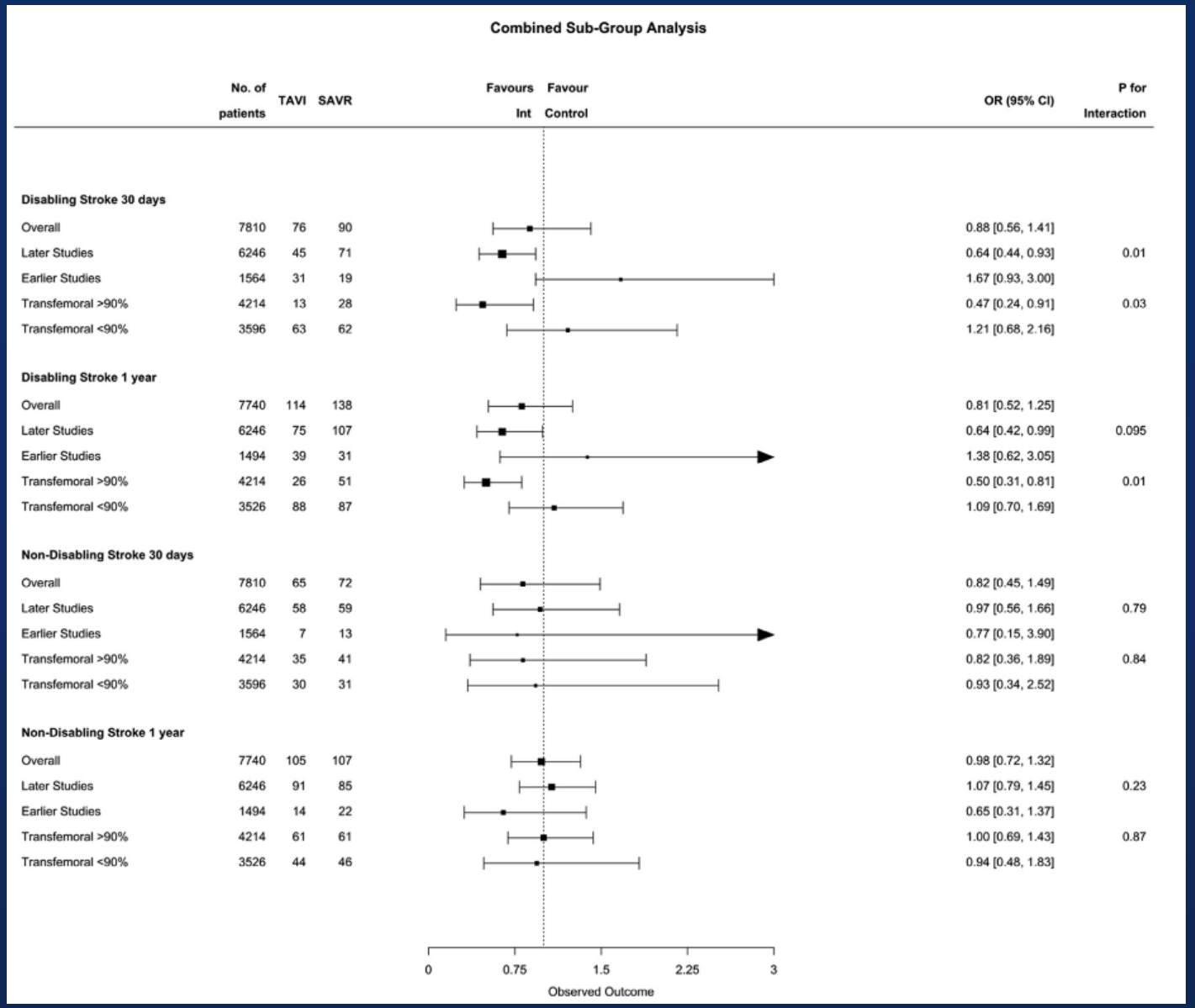
# Disabling and Non-disabling stroke 1 Year






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



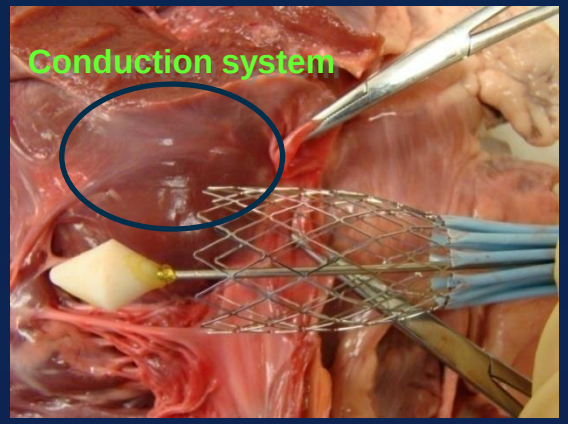

Padraig Synnott MB et al, Journal of Stroke and Cerebrovascular Diseases, Vol. 30, No. 9 (September), 2021:105927

# Conduction Disturbance

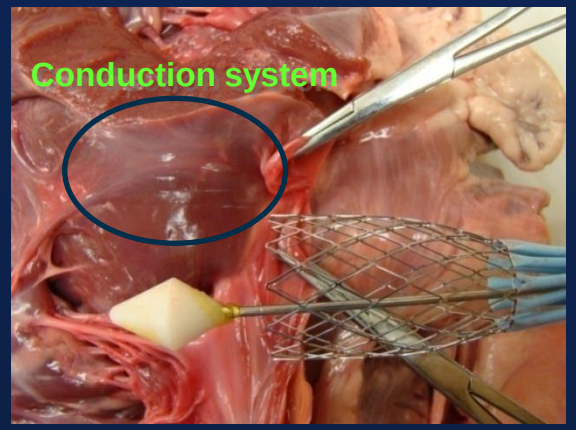
## Type

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

## Depth of Implantation

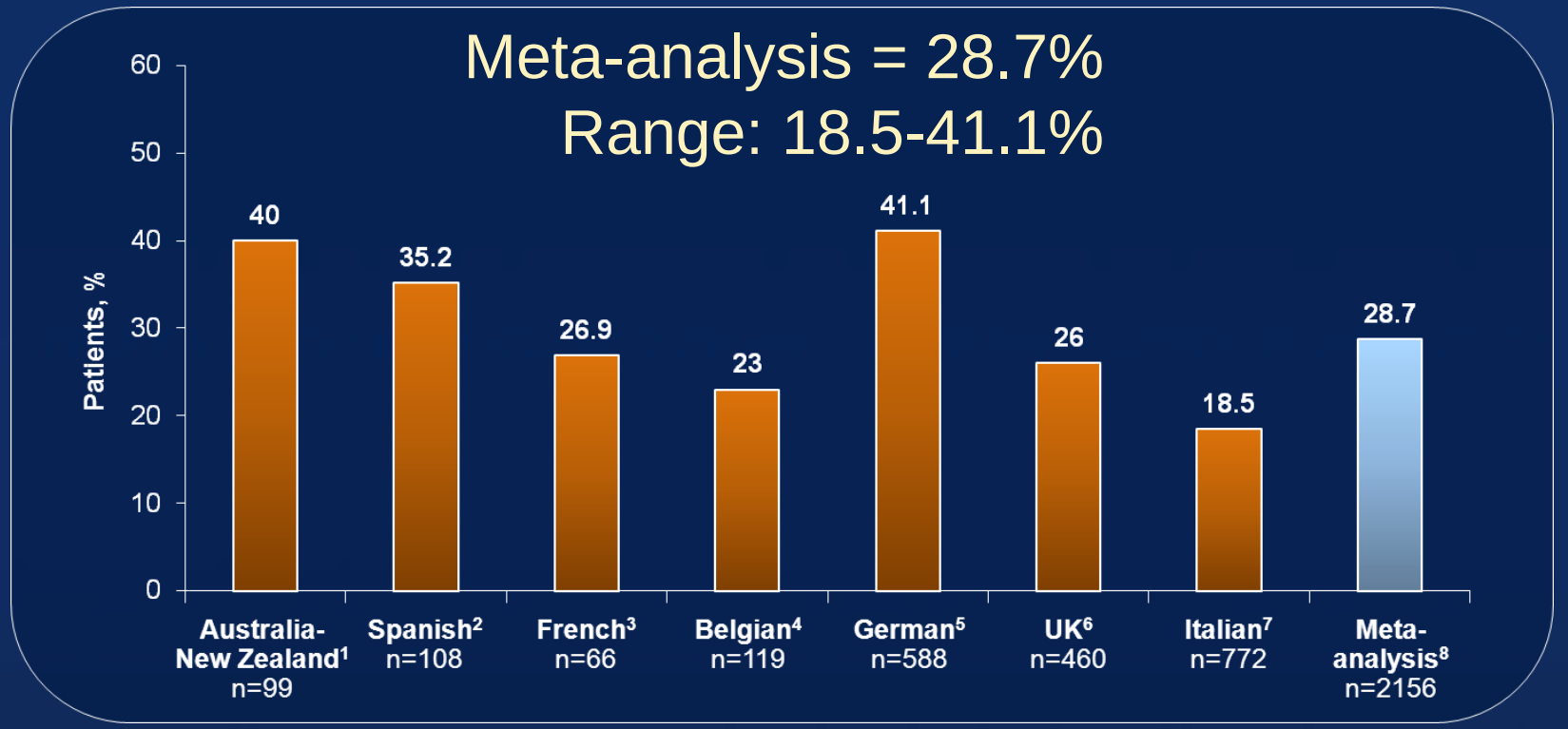



15mm - past annulus




5mm - past annulus

# CoreValve Meta-analysis : PPM

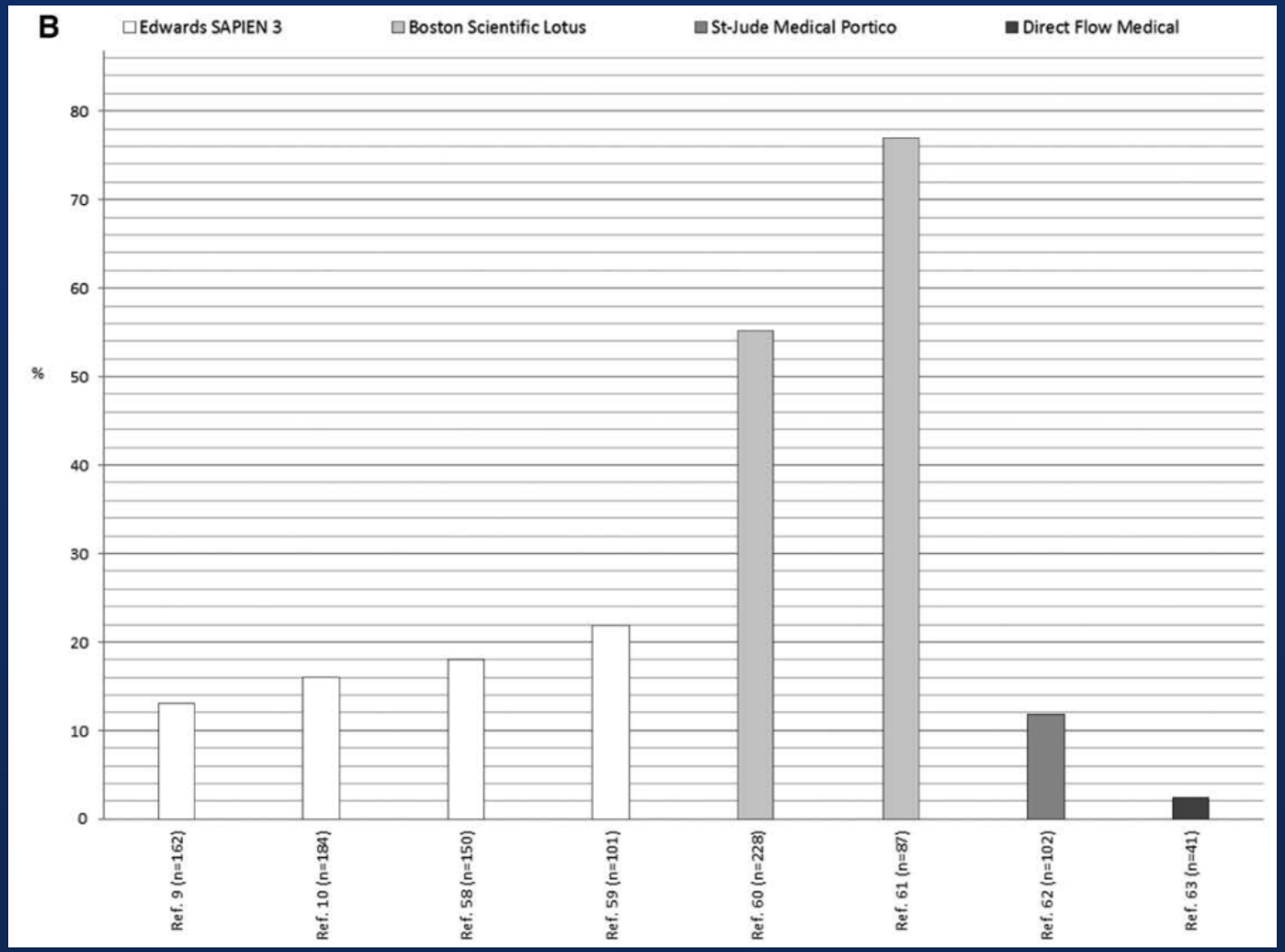




1. Meredith IT. The Australia-New Zealand Medtronic CoreValve® Registry: outcomes in inoperable and high risk AS patients. Presented at: TCT. 2010.
2. Avanzas P, et al. *Rev Esp Cardiol*. 2010;63:141-148.
3. Eltchaninoff H. French Registry. TAVI facts, figures and national registries. Presented at: EuroPCR; 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

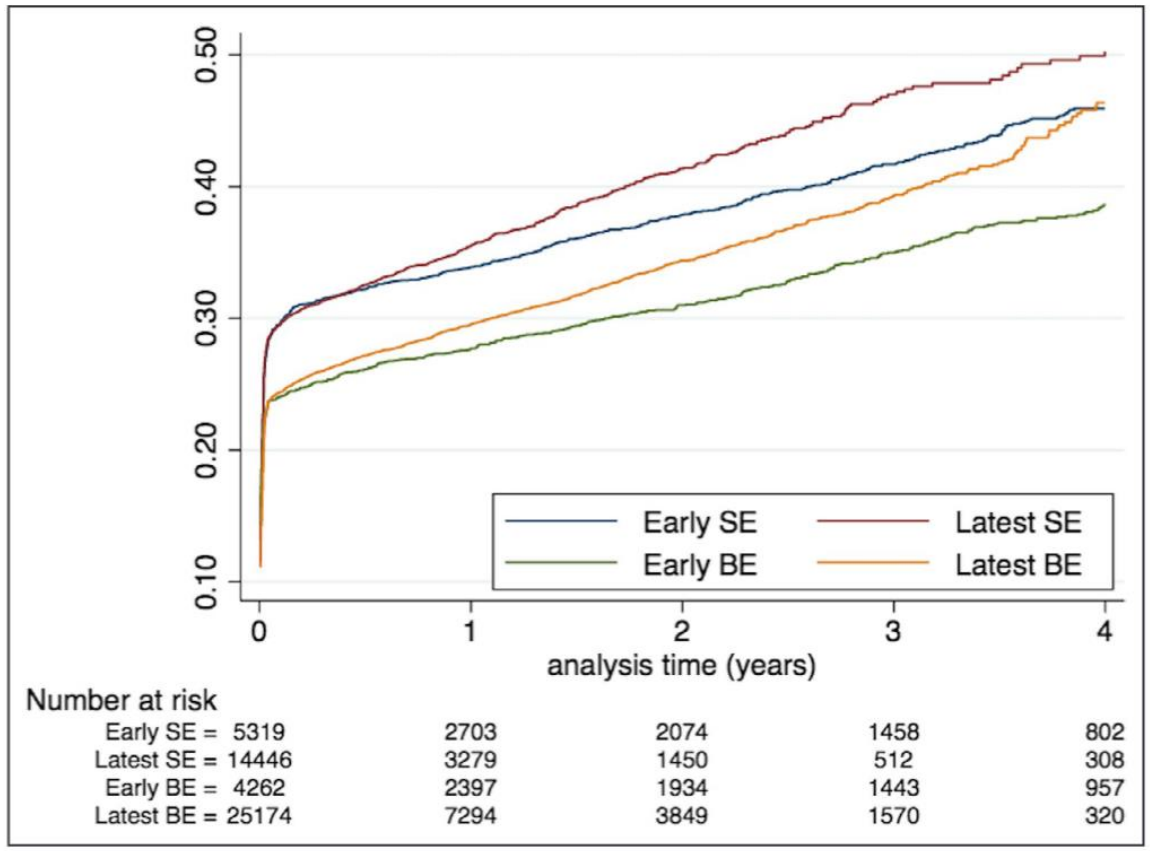



**Figure. Incidence of permanent pacemaker implantation in patients treated with TAVR, according to type and generation of device.**
BE indicates balloon-expandable; Early BE, Edwards Sapien XT; Early SE, Medtronic Corevalve; Latest BE, Edwards Sapien 3; Latest SE, Medtronic Evolut; SE, self-expandable;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

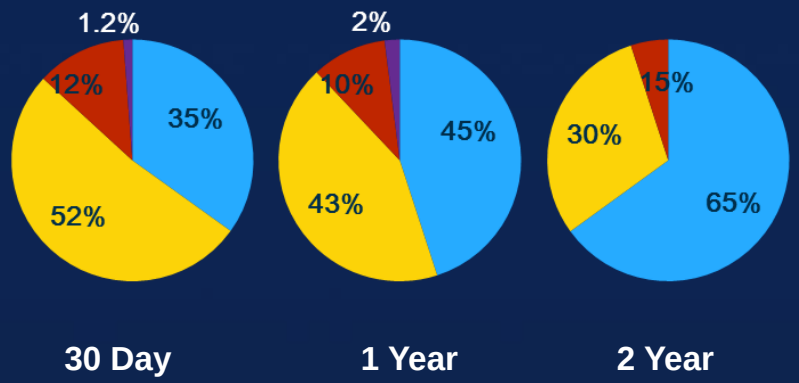
- BE technology was independently associated with lower incidence rates of PPI both at the acute and chronic phases than SE technology.
- Recent generations of TAVR were not independently associated with different rates of PPI than early generations during the overall follow-up.

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

# Para-valvular Leak

## Incidence of AR

**PARTNER Trial**



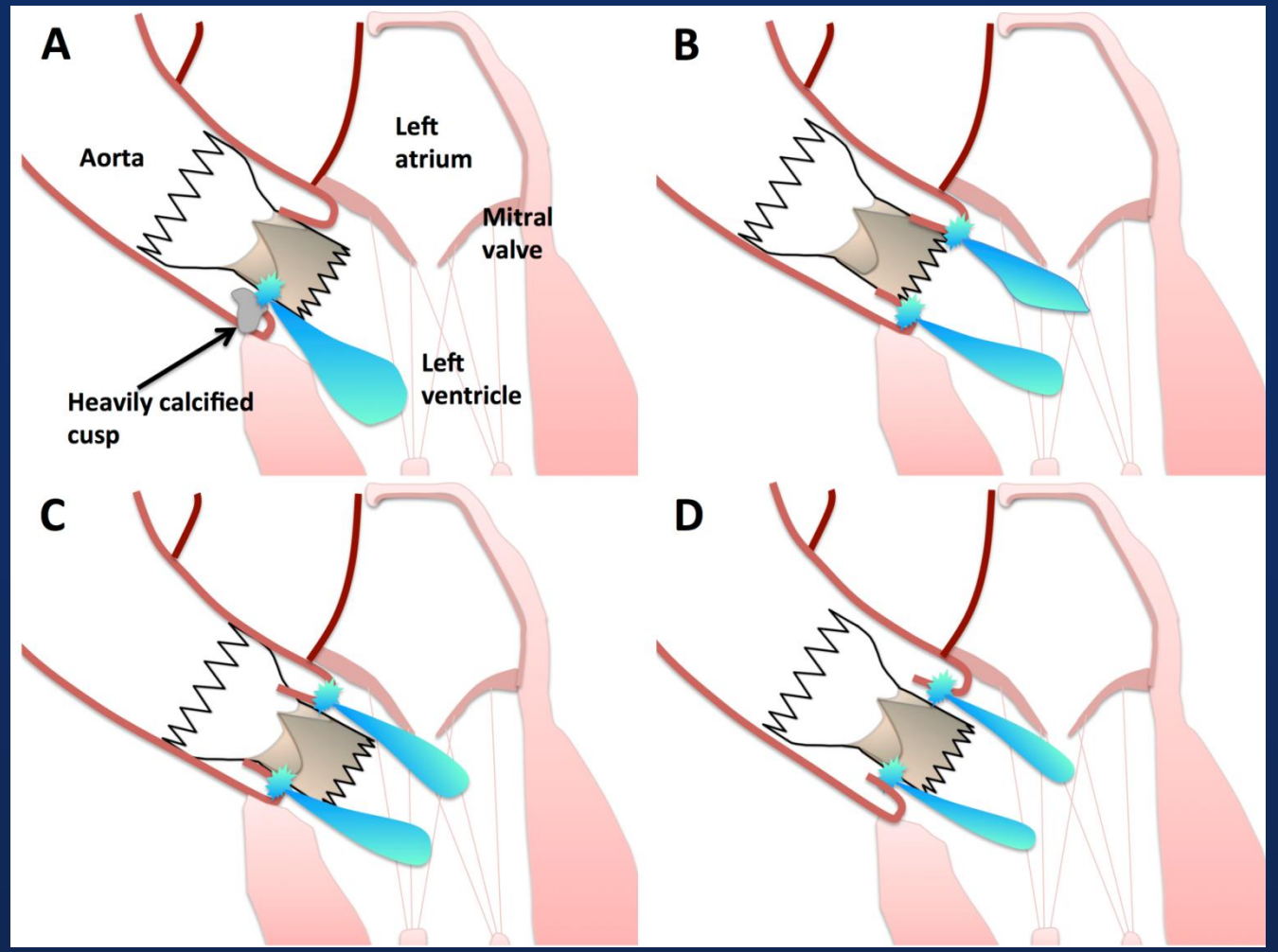

## Mechanism

- **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).**

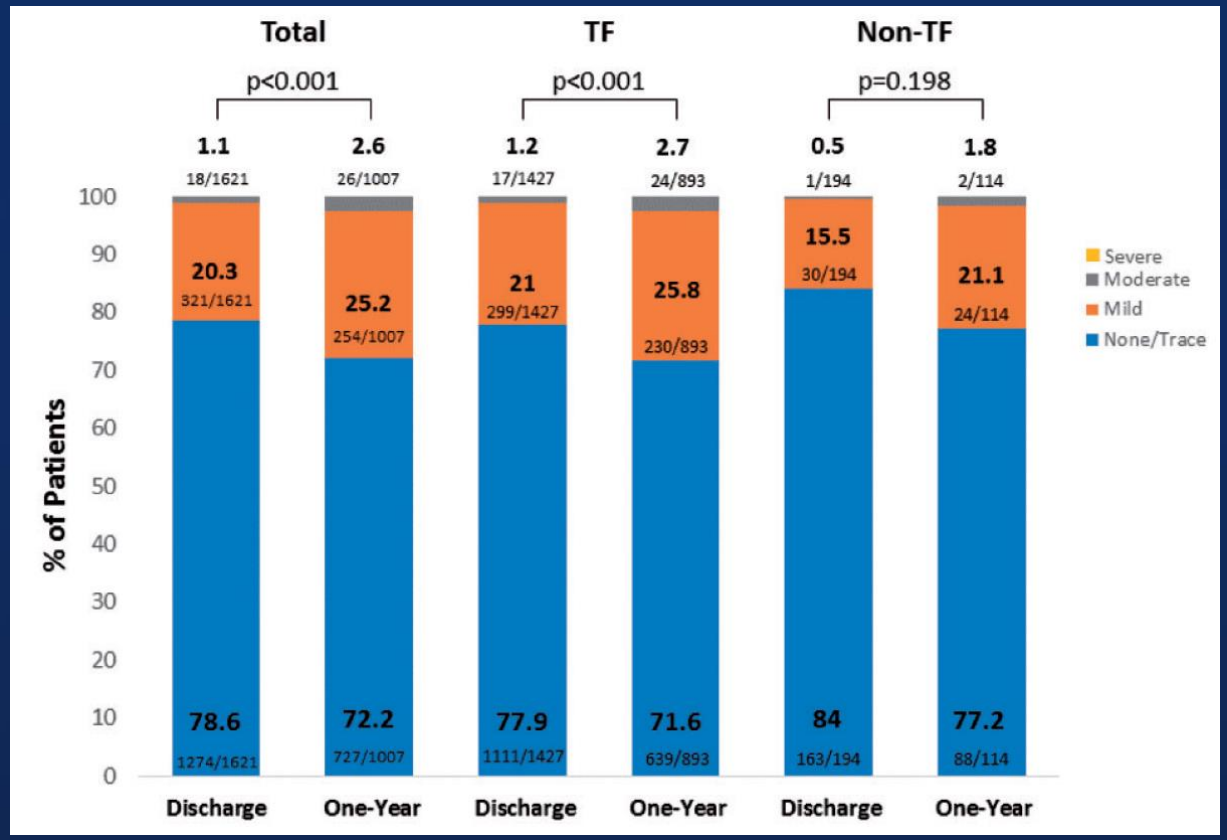
- Incidence of moderate/severe AR was 11.7%
- More common with CoreValve than with Edwards(16.0% vs. 9.1%; *P* = 0.005)
- Moderate/severe AR increased mortality at 30 days (OR 2.95; 95% CI 1.73-5.02) and 1 year (HR 2.27; 95% CI 1.84-2.81)
- Even mild AR was linked to mortality in some studies
- Predictors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

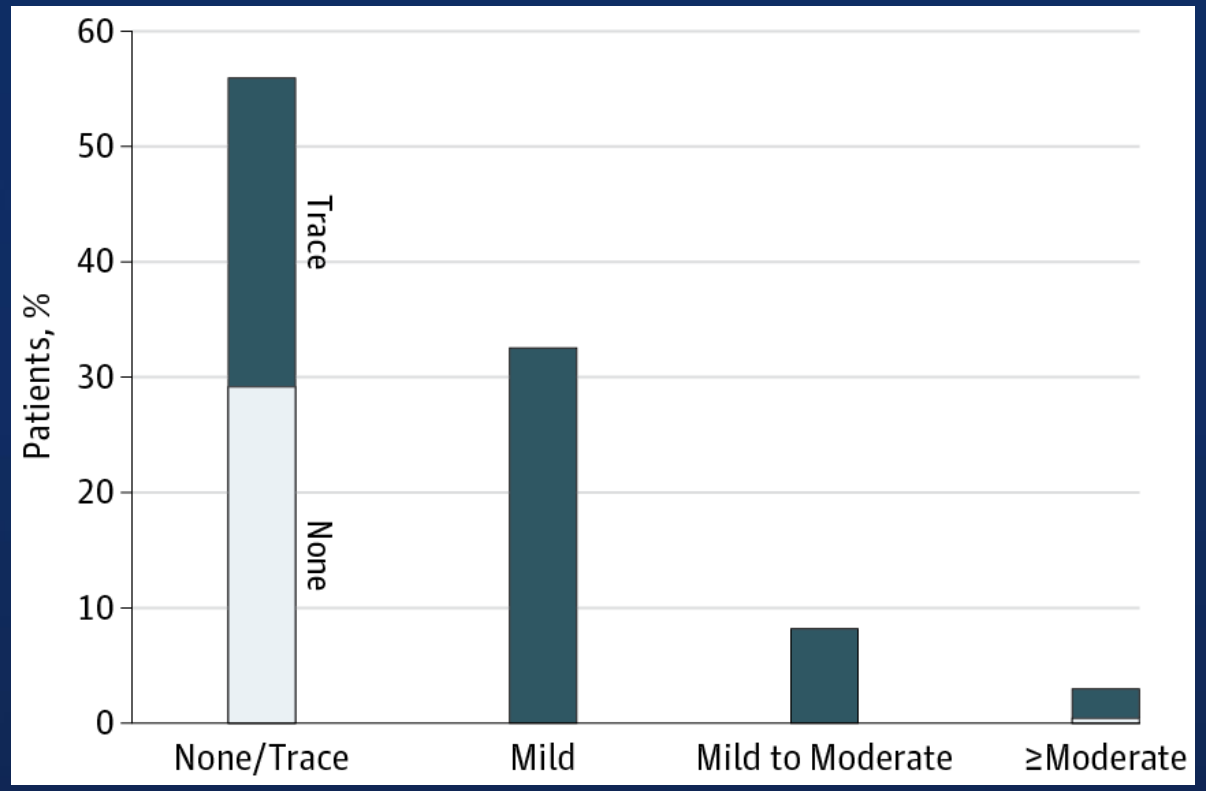
# SOURCE 3 : 1yr outcome

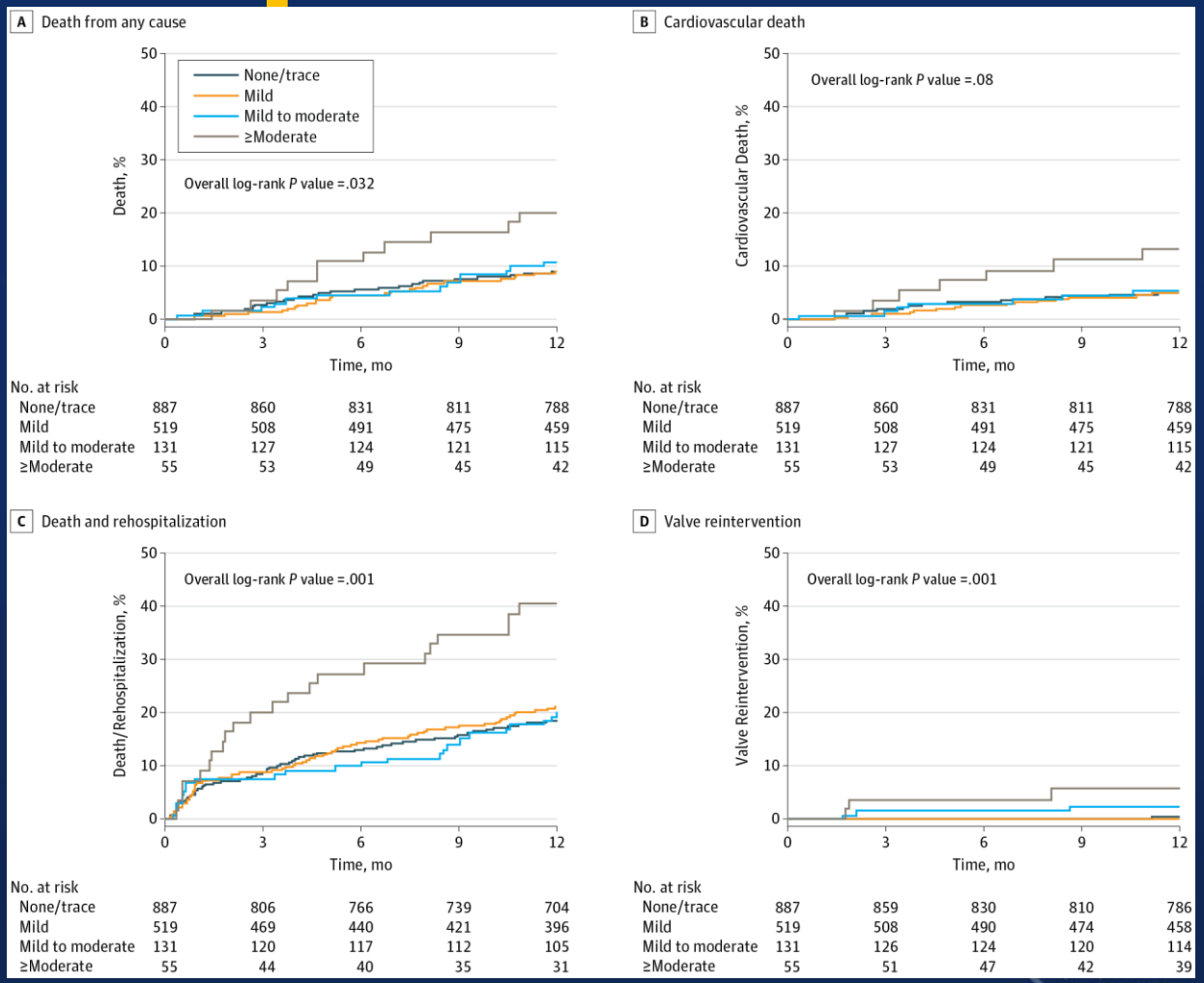
## PVL (mod-severe) for 1yr mortality : HR 0.09 (0.00, NA), p = 0.97




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

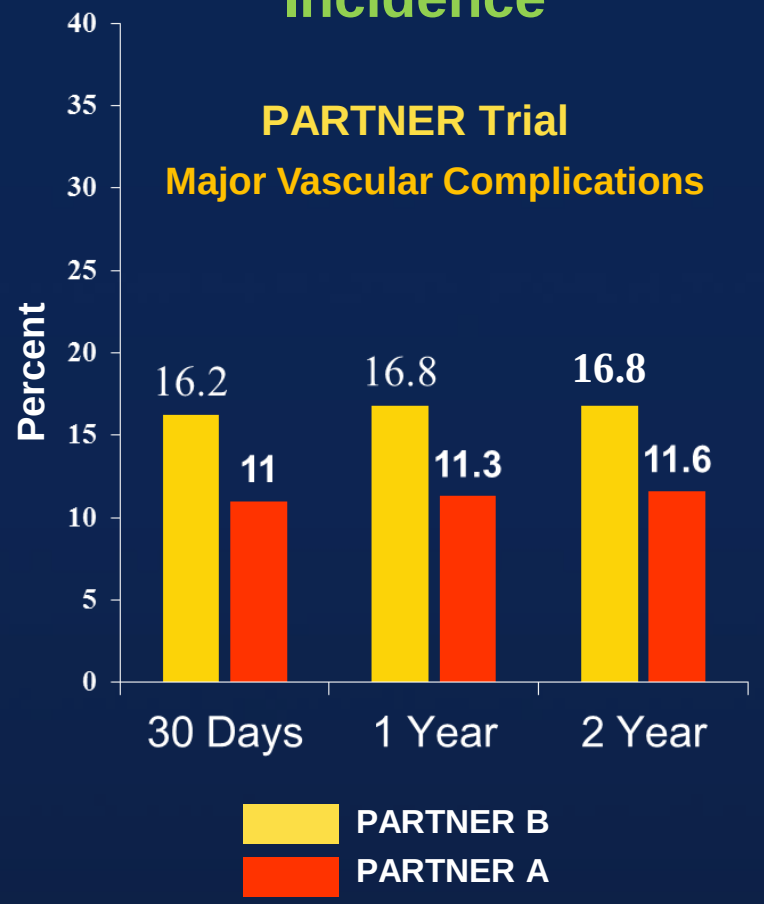
## Type

- 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*

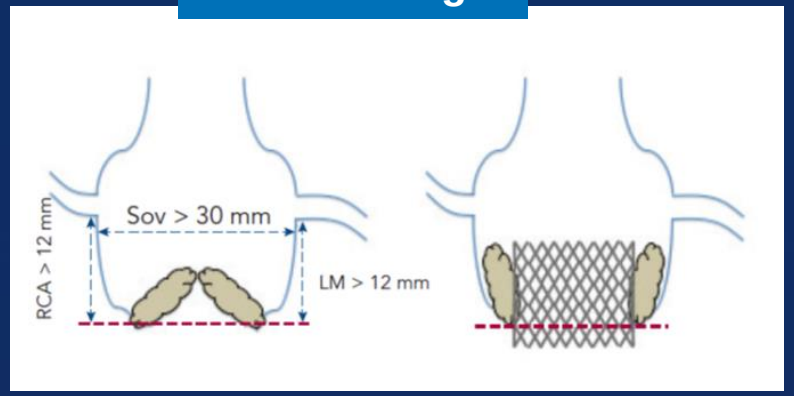
- Women
- Low Coronary Height (<10mm to <12mm)
- Shallow Sinus of Valsalva (<30mm)
- Long Leaflet
- Left Coronary Artery
- Bulky Calcification
- Valve Implantation Height
- Device (Balloon Expandable)

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

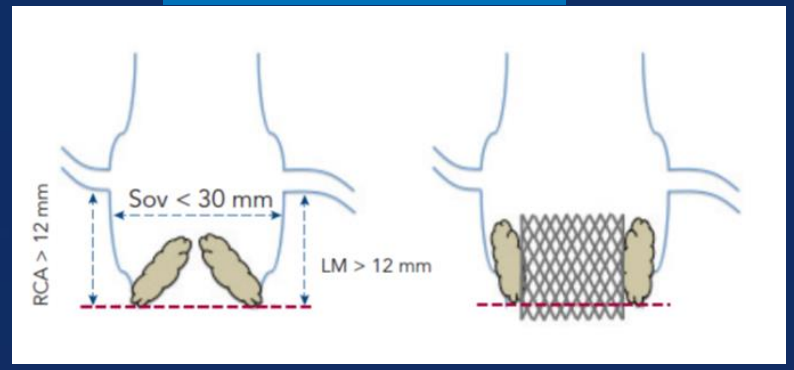
Riberiro HB, et al. J Am Coll Cardiol. 2013 Oct 22;62(17):1552-62

# Aortic Root Scenarios

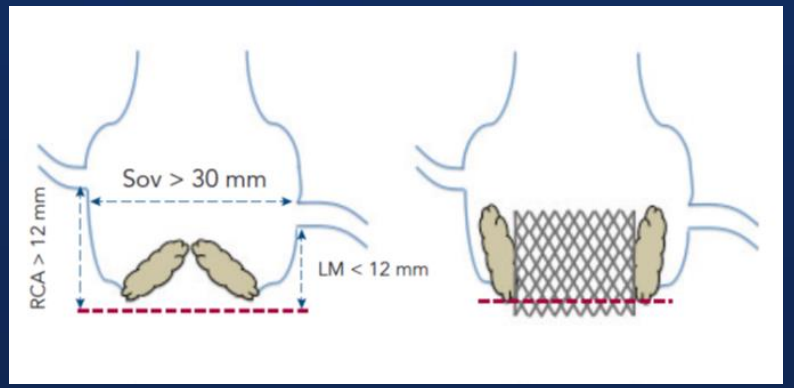
## Wide and High



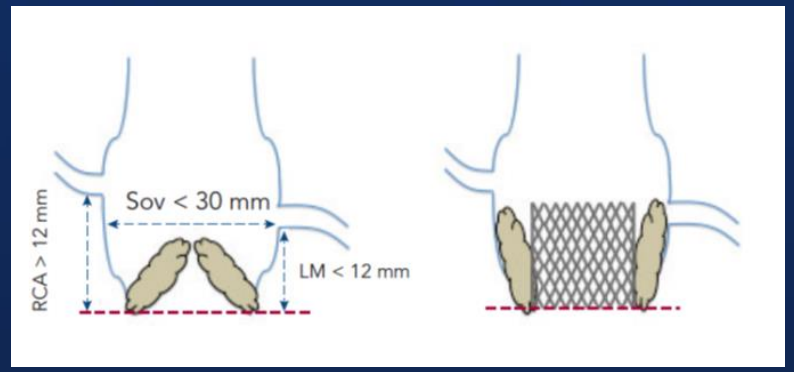

## Shallow and High




## 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%)

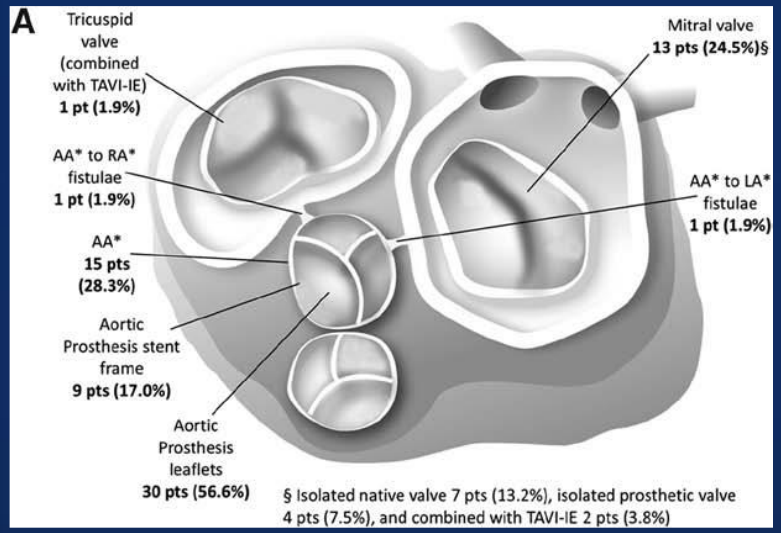
S. aureus (21%), Enterococci (21%)

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



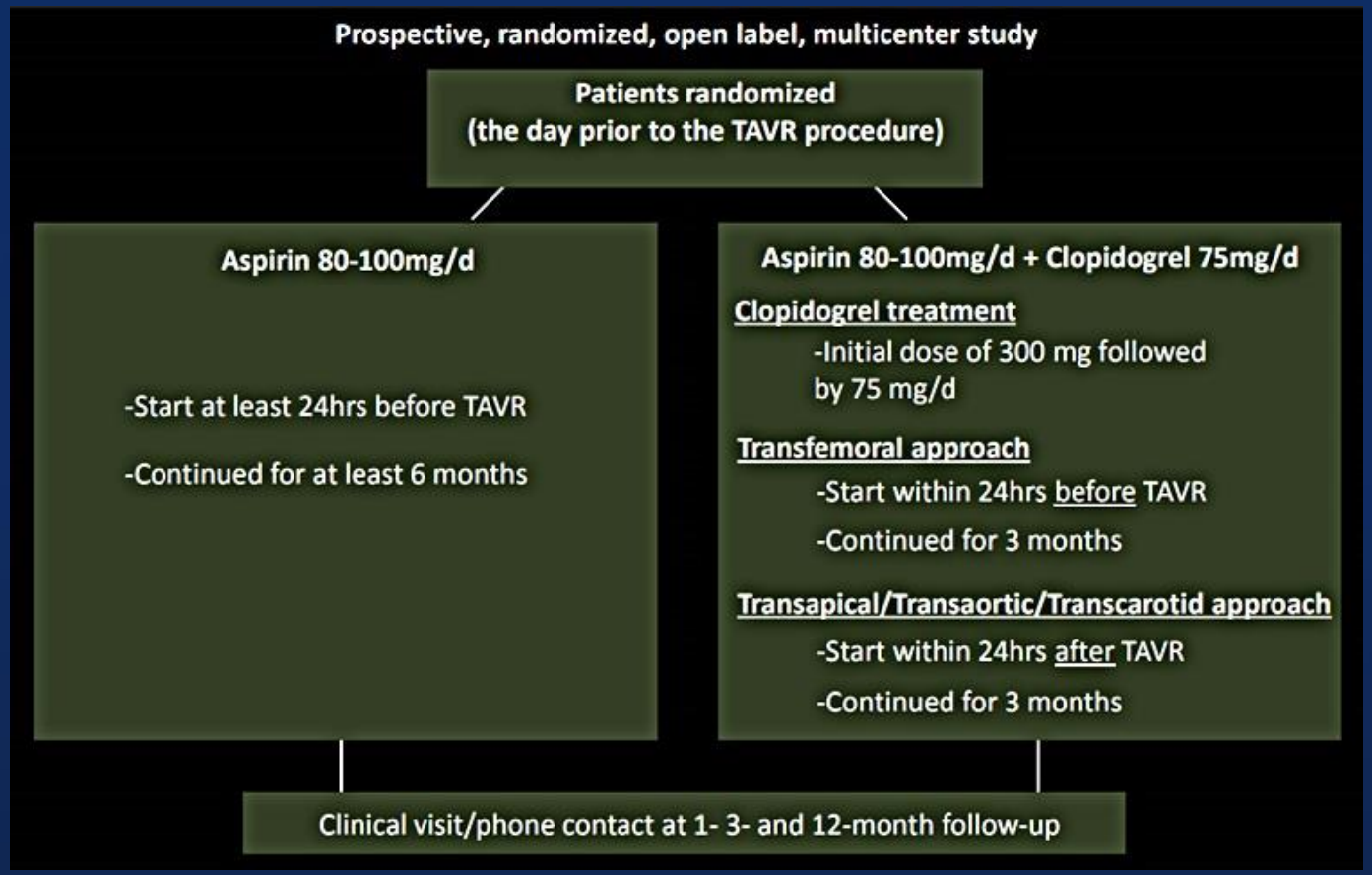

*AA; Ascending Aorta
LA; Left Atrium
RA; Right Atrium

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

# Antithrombotics after TAVR

# ARTE Trial

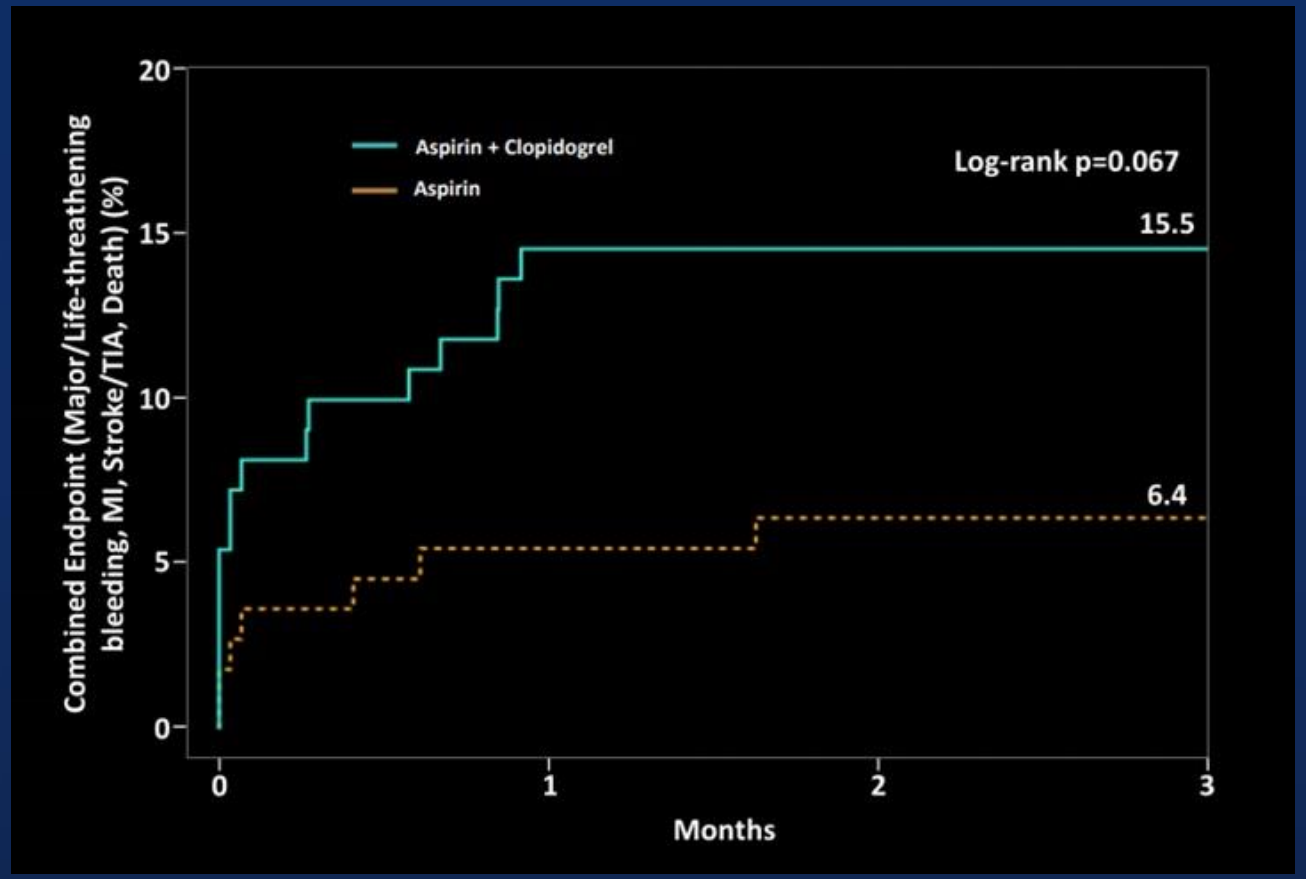
## Aspirin alone vs. Aspirin + clopidogrel




Josep Rodes-Cabau et al. 2017 EuroPCR

# ARTE Trial

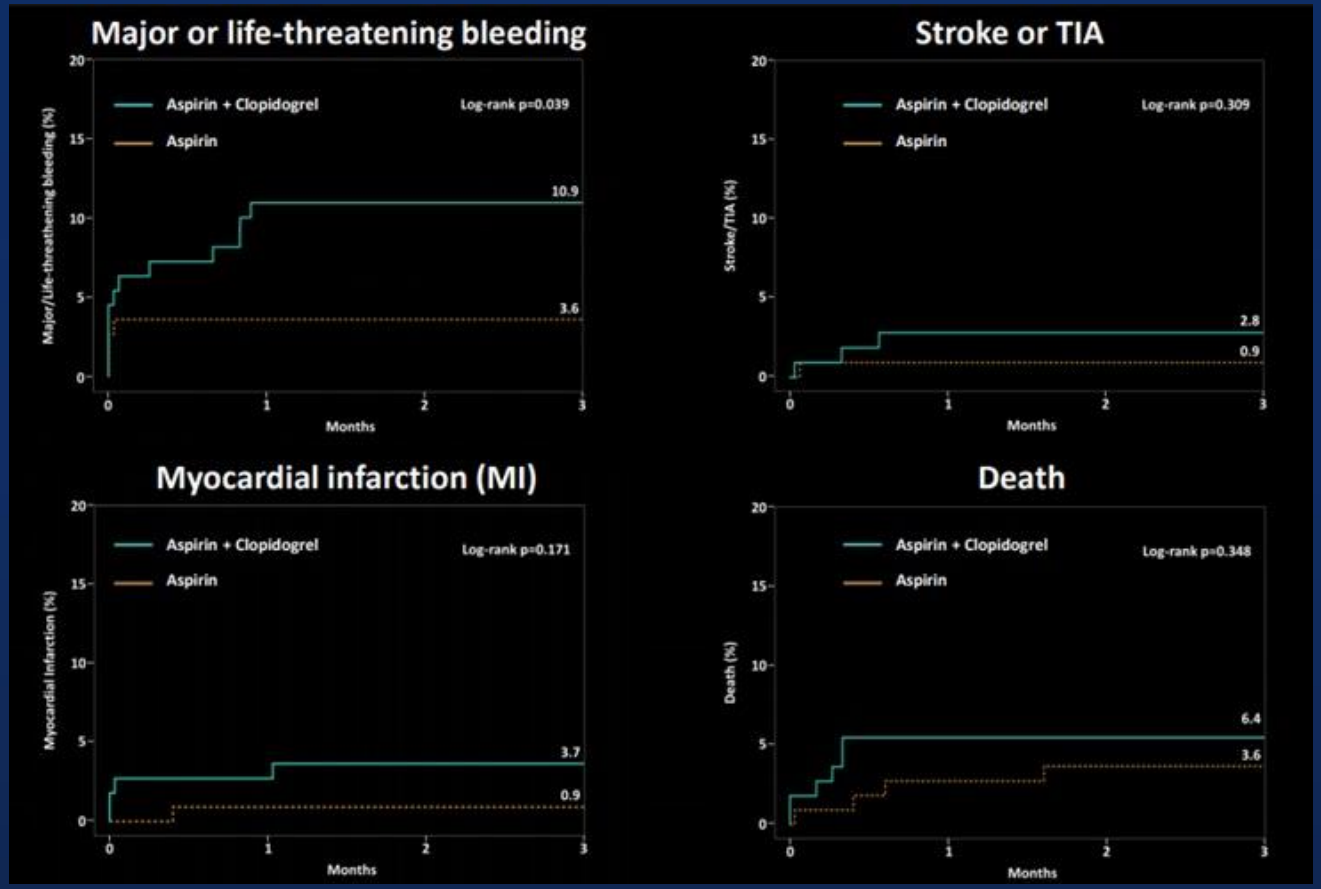
## Aspirin alone vs. Aspirin + clopidogrel




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

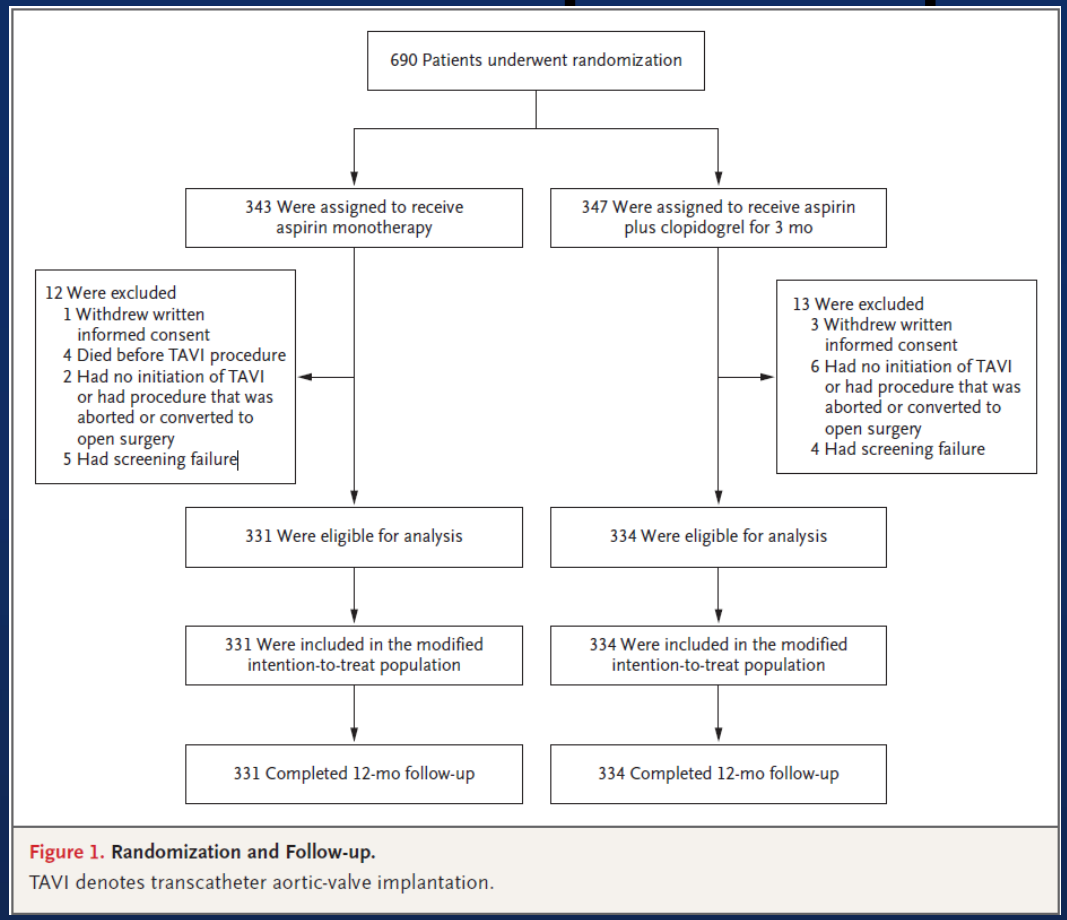
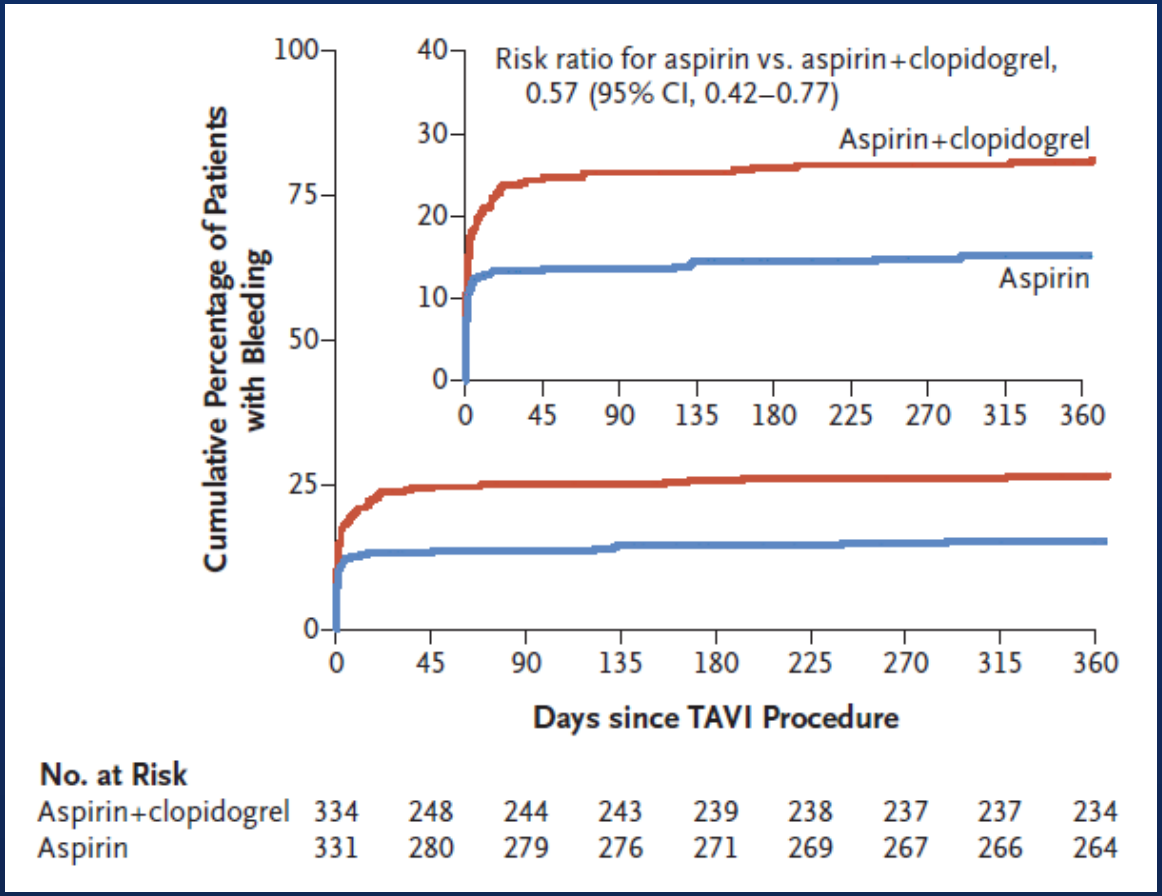



**Figure 1. Randomization and Follow-up.**
TAVI denotes transcatheter aortic-valve implantation.

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

# POPular TAVI Trial

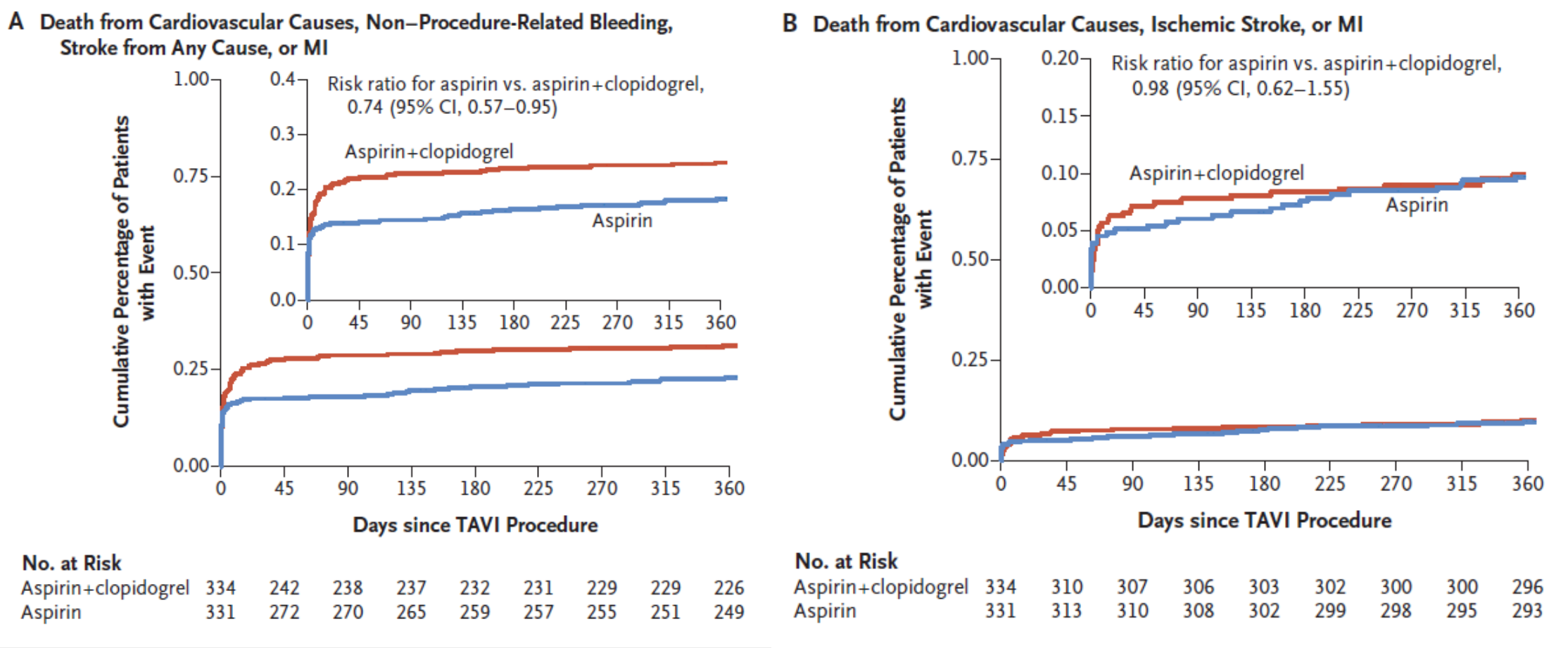
## Aspirin alone vs. Aspirin + clopidogrel




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

# POPular TAVI Trial

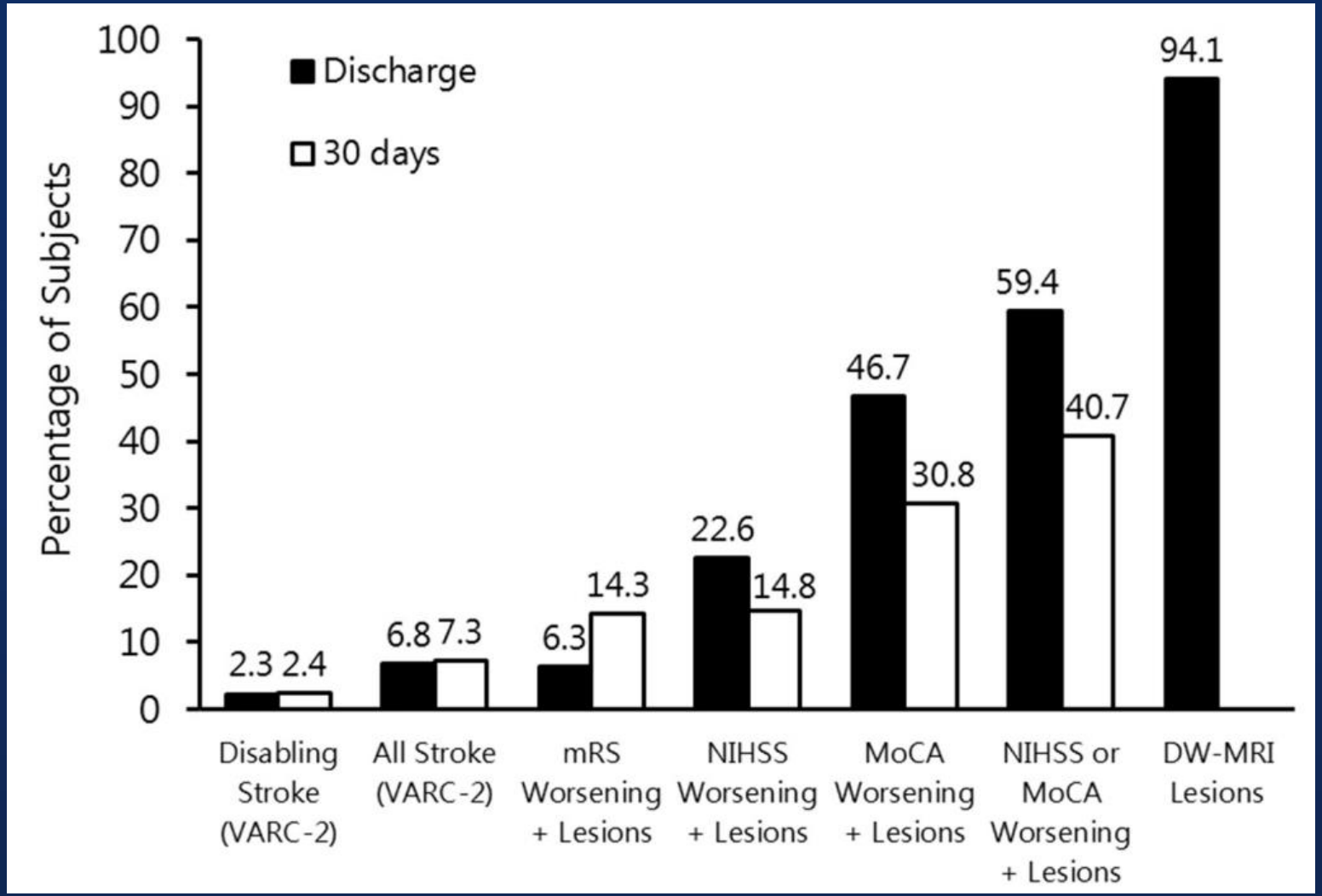
## Aspirin alone vs. Aspirin + clopidogrel




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

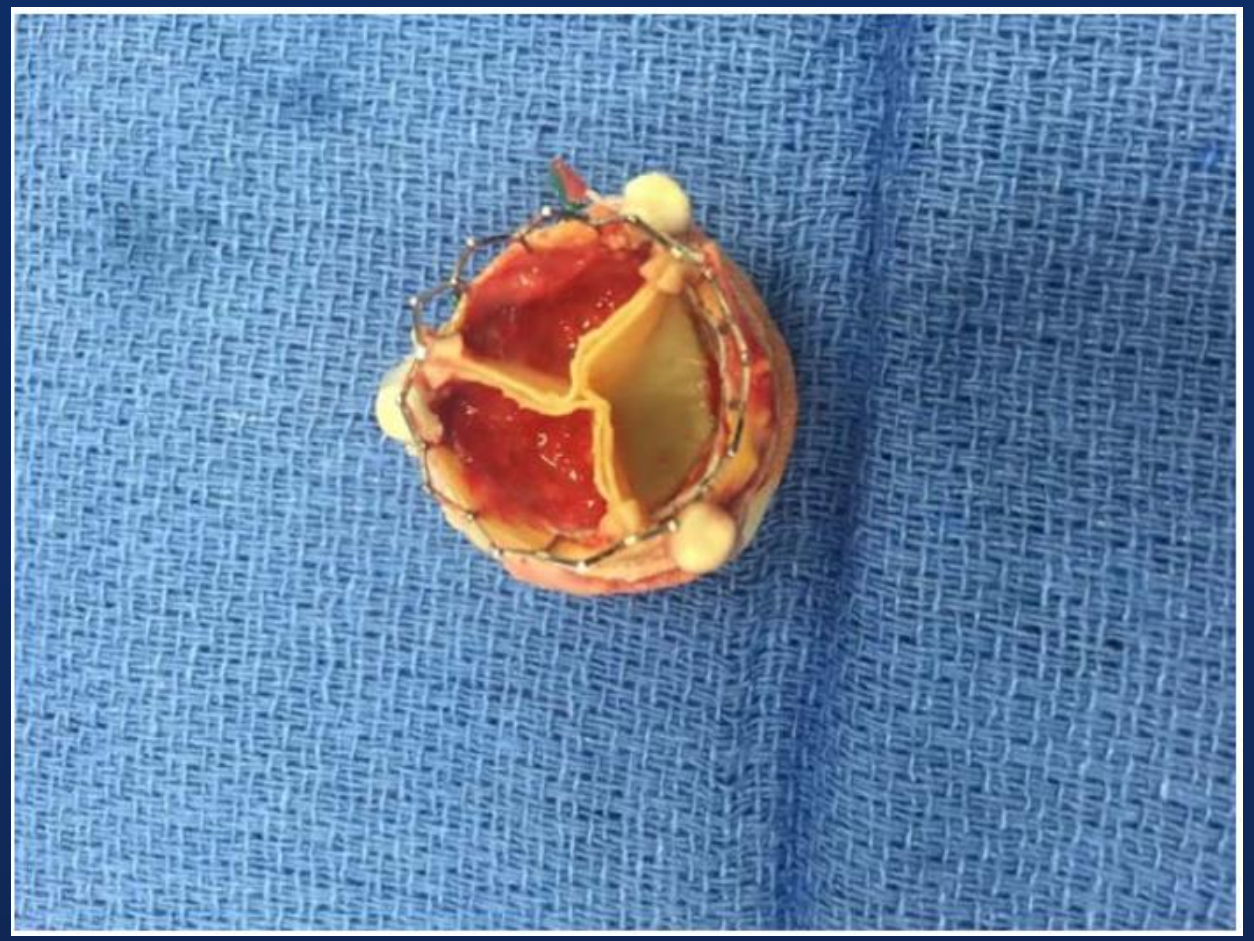
# Leaflet Thrombosis

# Neurological injury after TAVR From Neuro-TAVI trial




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

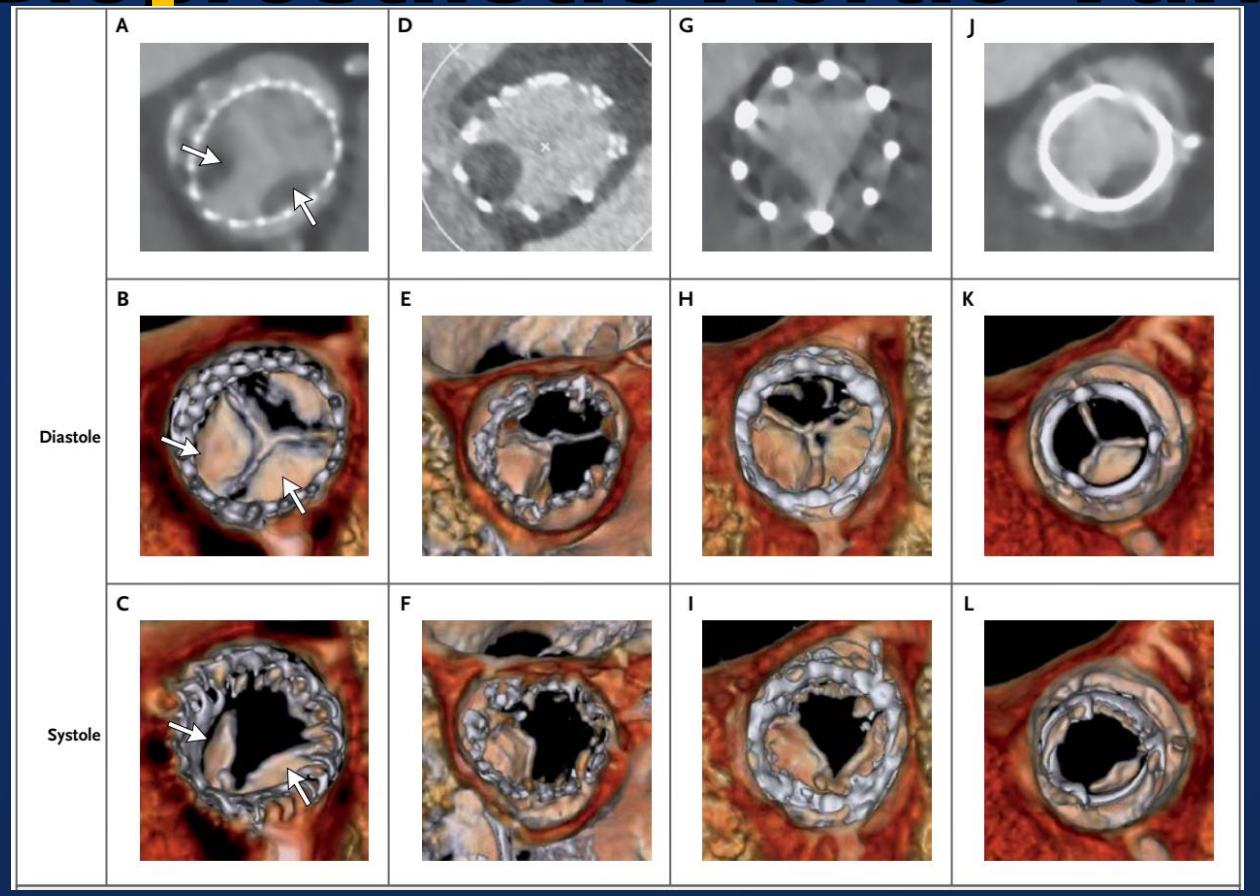
# Excised TAVR with thrombosis





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

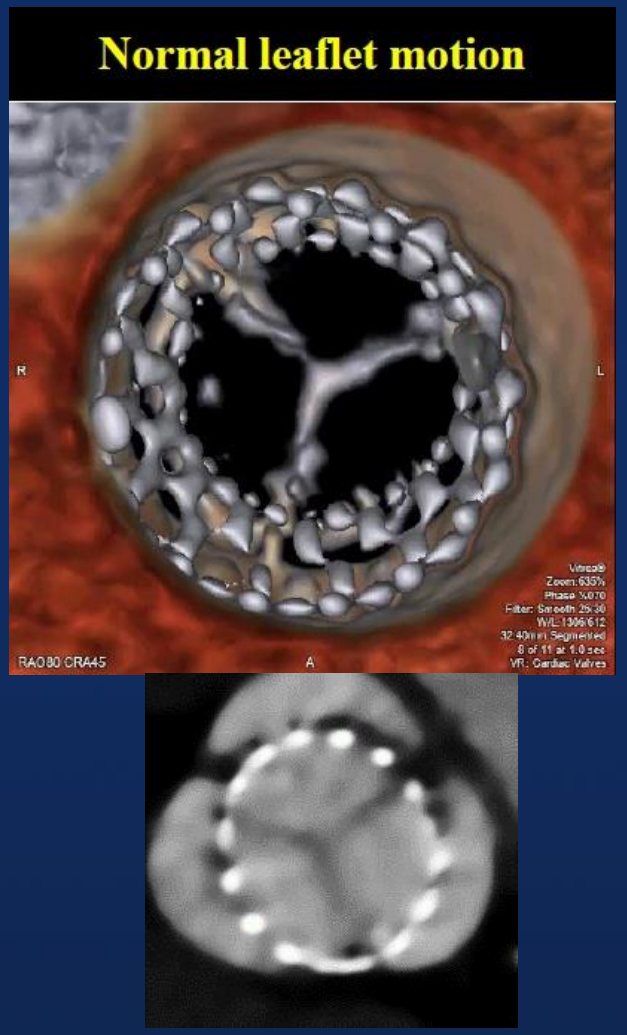
| Authors | Diagnostic Method | Procedure | Finding | Patients, n | Finding, n (%) | Comment |
|---|---|---|---|---|---|---|
| Makkar et al[1] | MDCT | TAVR | Reduced leaflet motion | 55 | 22 (40) | Surveillance |
| | MDCT | SAVR | Reduced leaflet motion | 132 | 17 (13) | For cause |
| De Marchena et 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 | 10 099 | 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 |

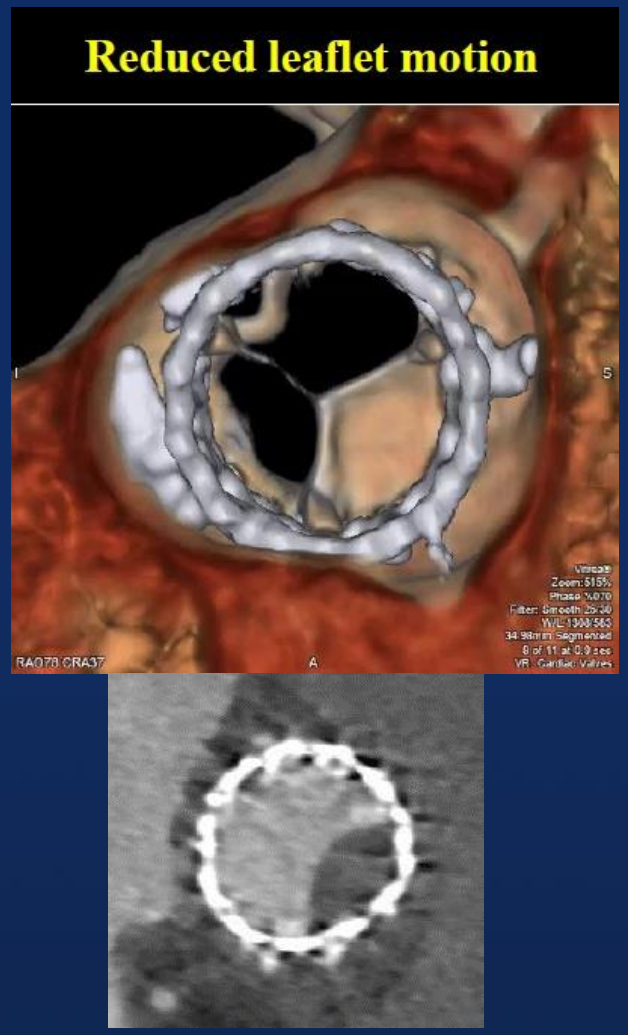


David R. Holmes and Michael J. Mack. Circulation 2017.

# Reduced leaflet motion

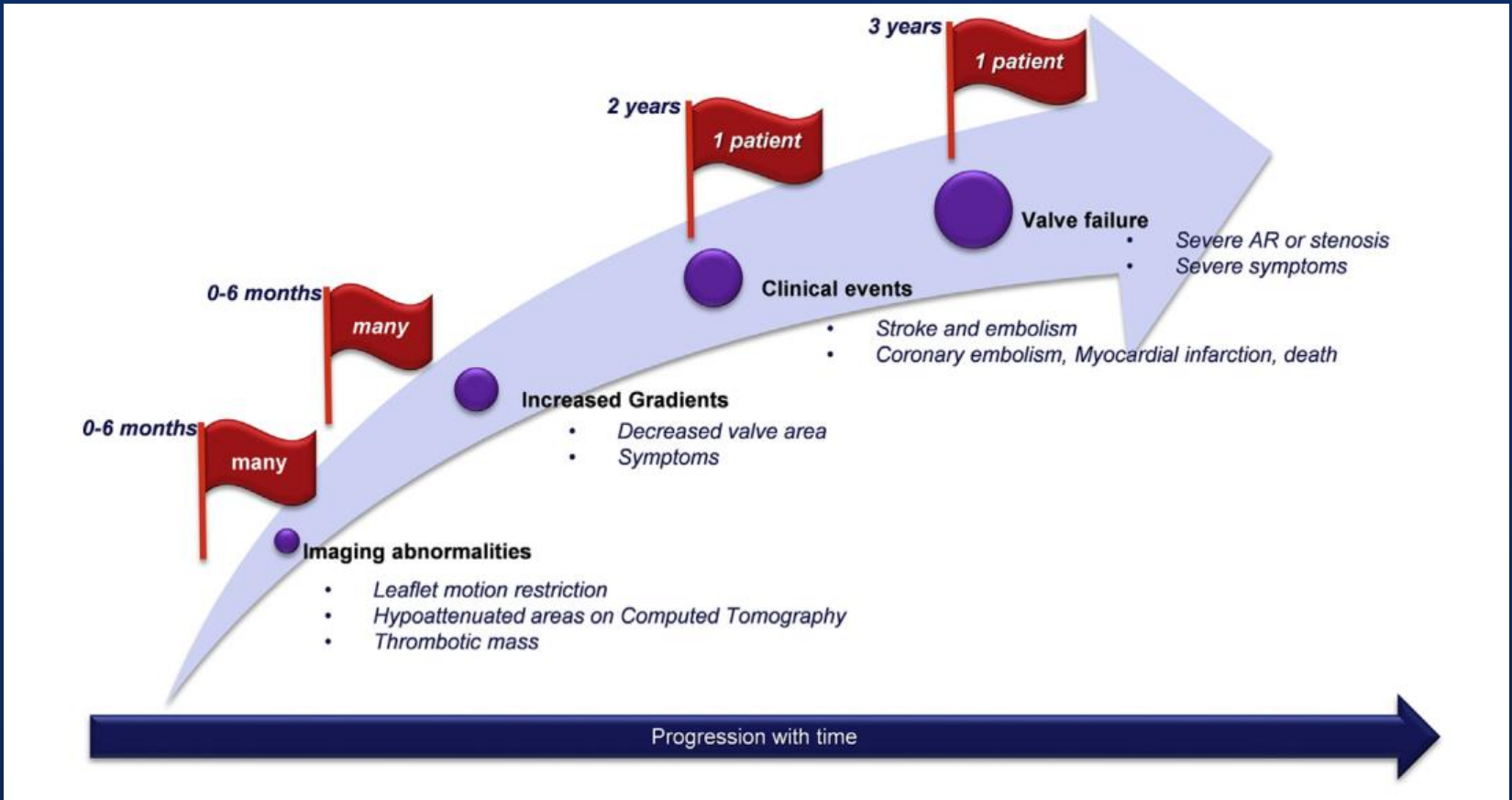
## At least 50% restriction of leaflet motion of at least 50%




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

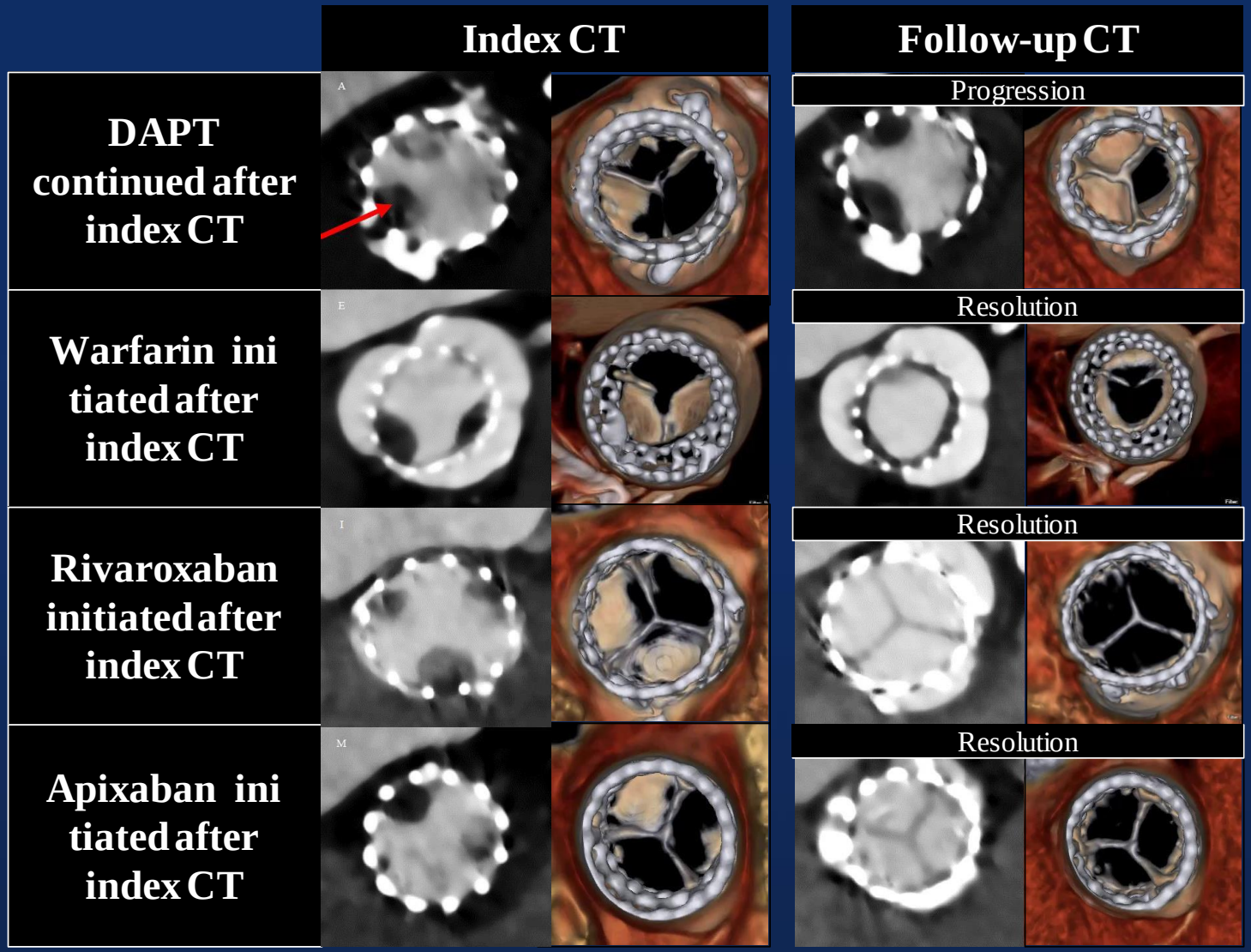
**TABLE 3** Predictors of Clinical Transcatheter Valve Thrombosis

| | 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

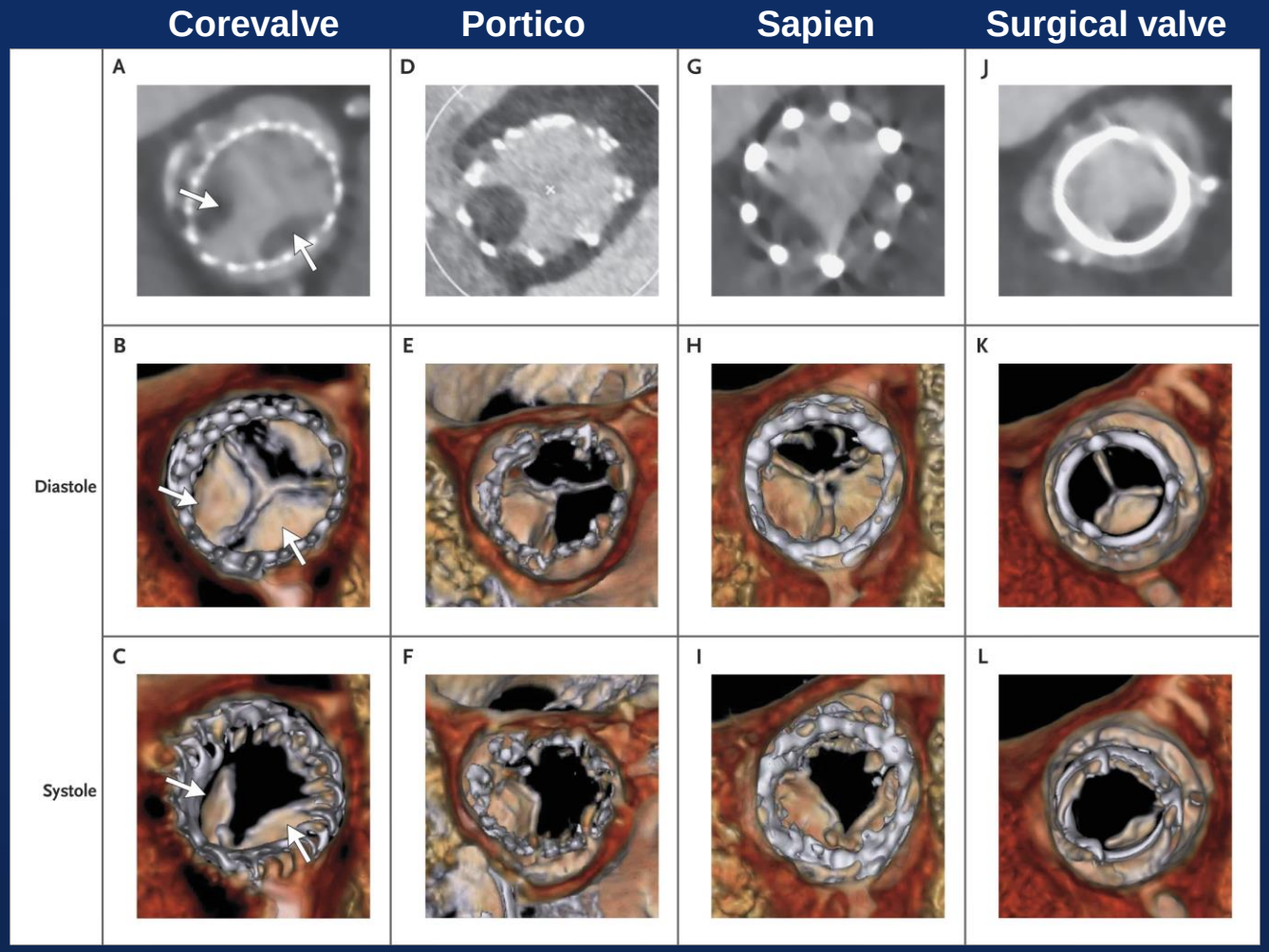
# Anticoagulation vs. DAPT




Chakravarty T, et al. Lancet 2017.

# Possible Subclinical Leaflet Thrombosis in Bioprosthetic Aortic Valves

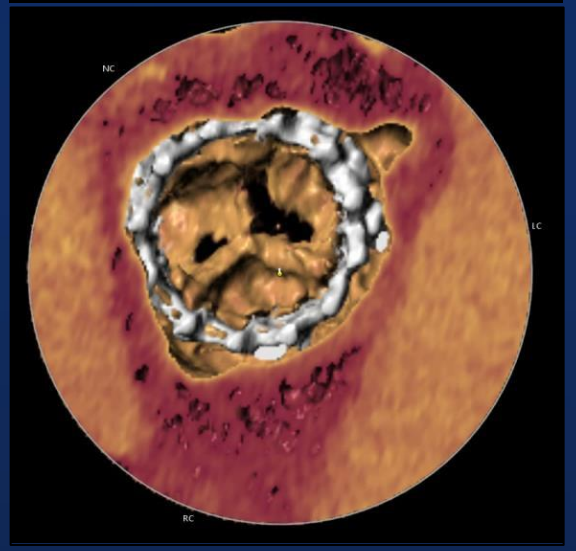
## Evidence of Reduced Leaflet Motion in Multiple Prosthesis Types



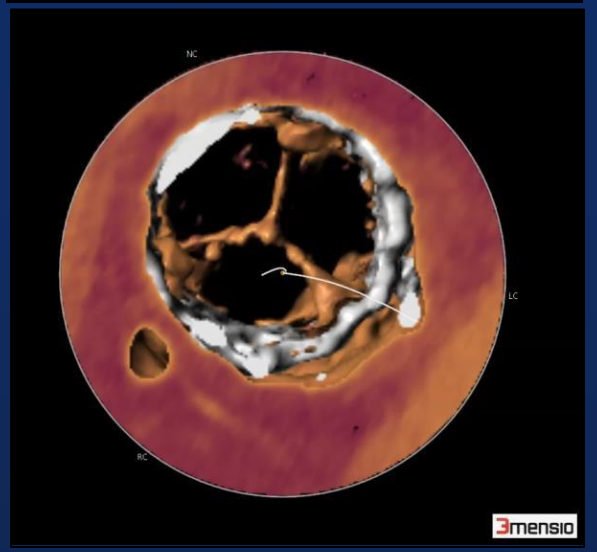

Makkar RR et al. N Engl J Med 2015;373:2015-2024

# Recurrence of Reduced Leaflet Motion Following Discontinuation of anticoagulation

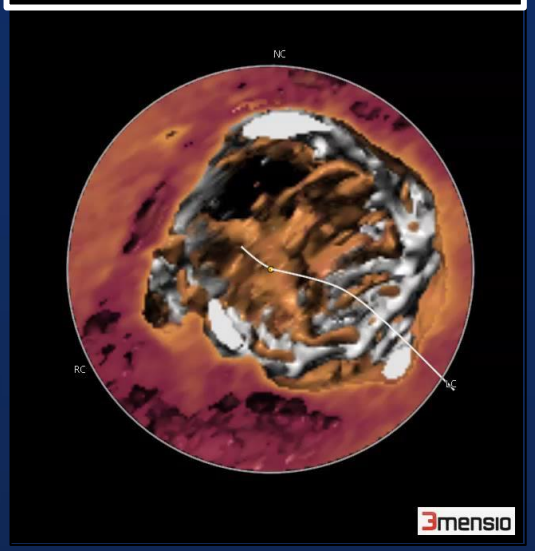
**Baseline**
Reduced leaflet motion




**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]

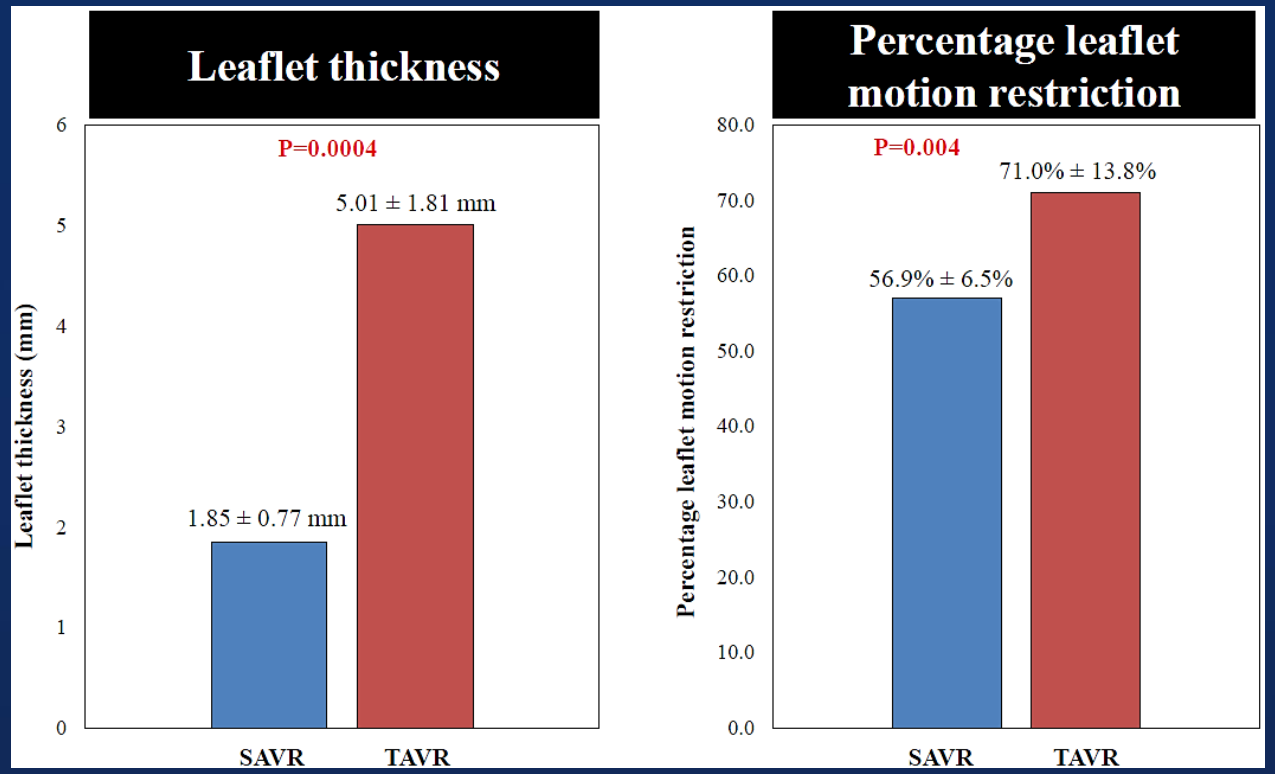
# Prevalence of reduced leaflet motion

Transcatheter vs. surgical bioprosthetic aortic valves: p=0.001

Reduced leaflet motion 106 (11.9%) patients

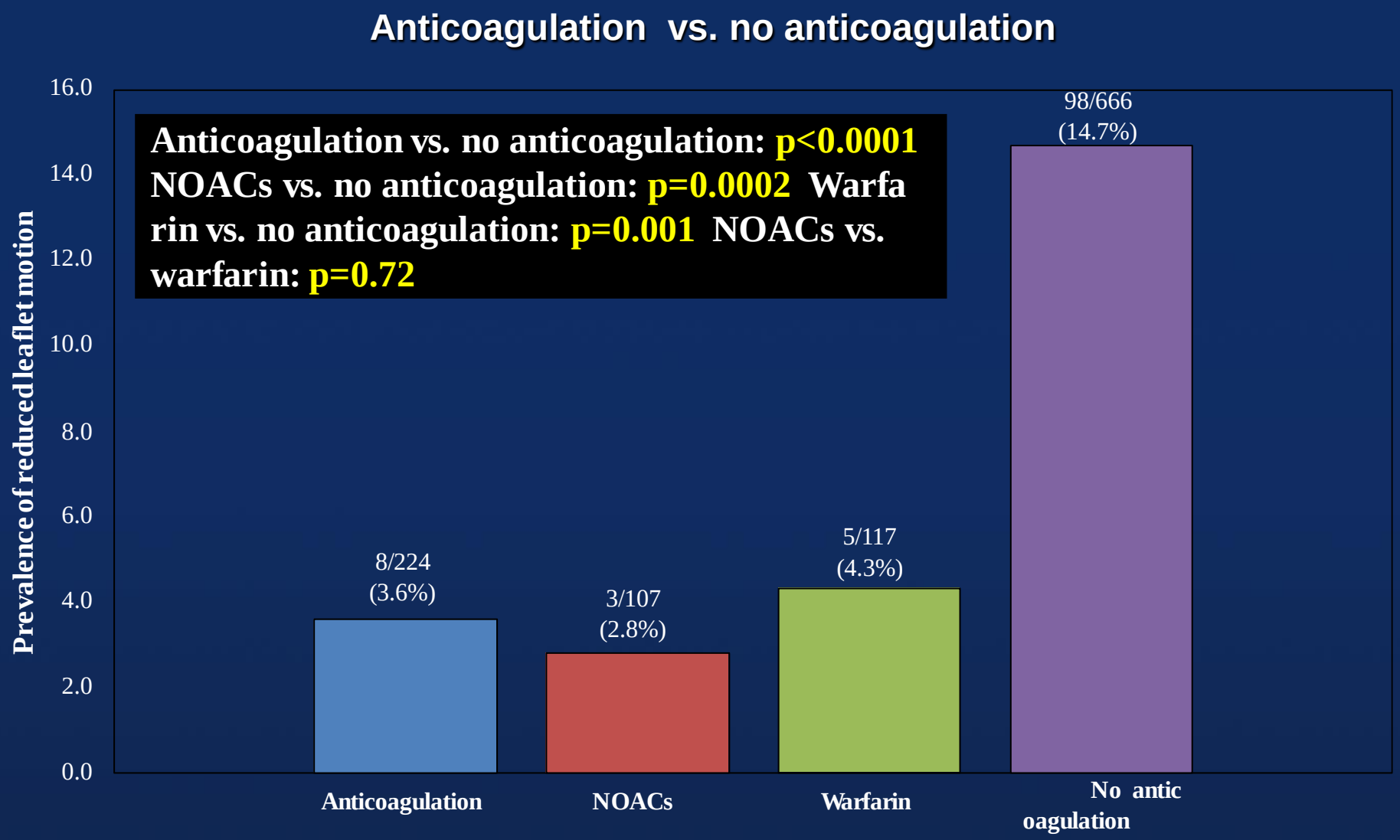
Transcatheter valves 13.4% (101 out of 752)

Surgical valves 3.6% (5 out of 138)



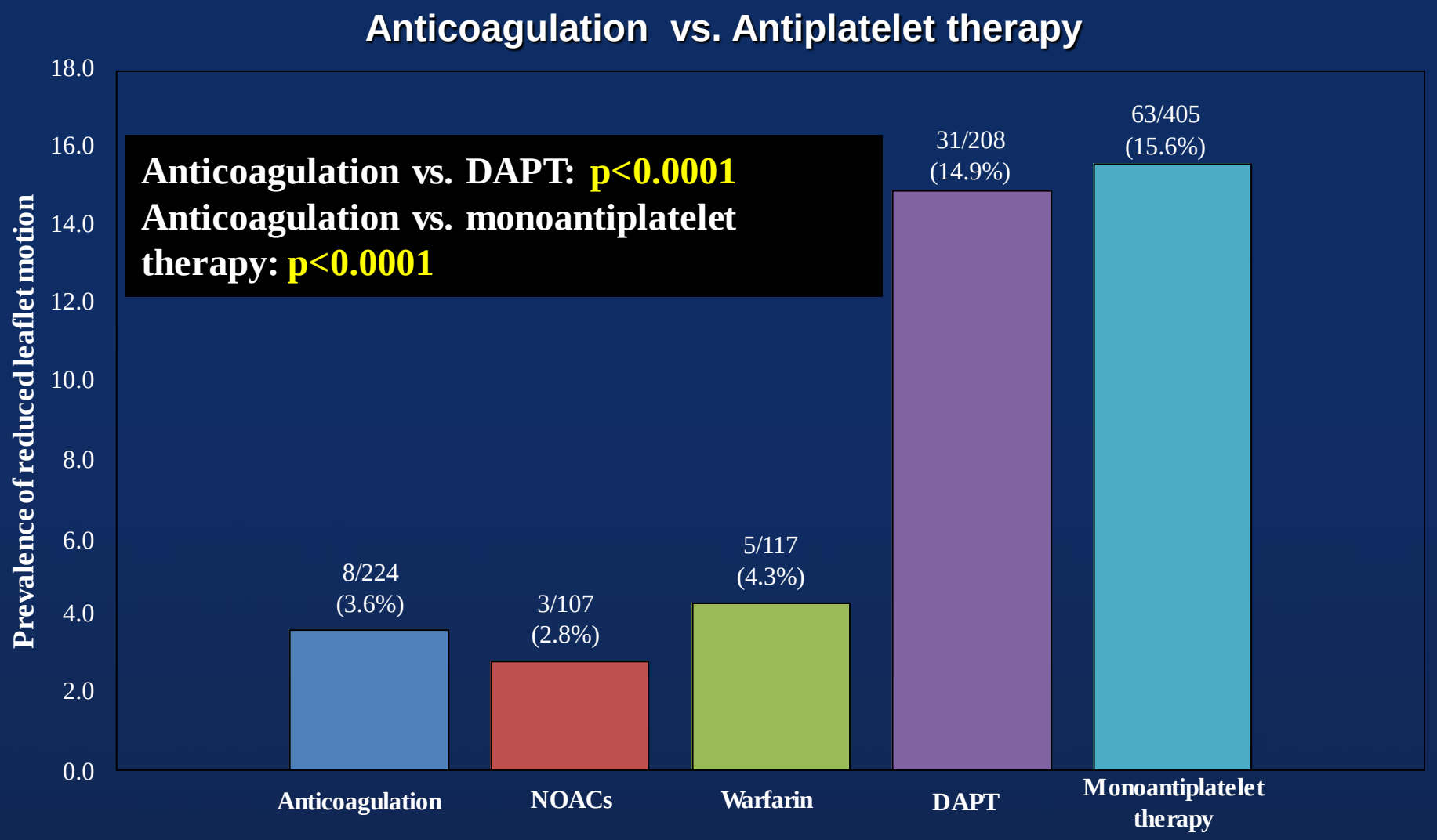

Chakravarty T, et al. Lancet. 2017 Mar 19. [Epub ahead of print]

# Anticoagulation and Reduced Leaflet Motion




Chakravarty T, et al. Lancet 2017.

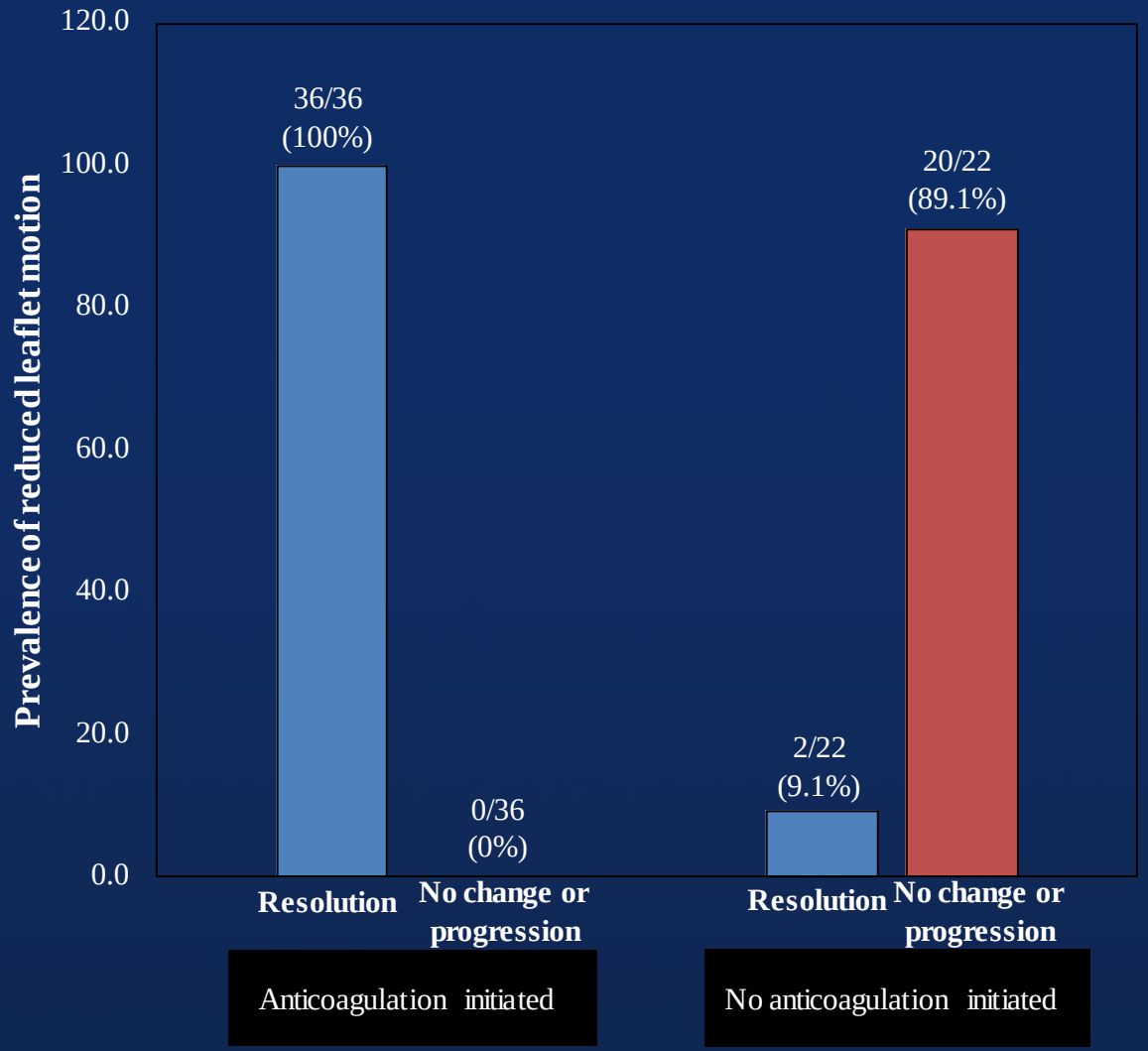
# Anticoagulation and Reduced Leaflet Motion






Chakravarty T, et al. Lancet 2017.

# Impact of Initiation of Anticoagulation on Reduced Leaflet Motion

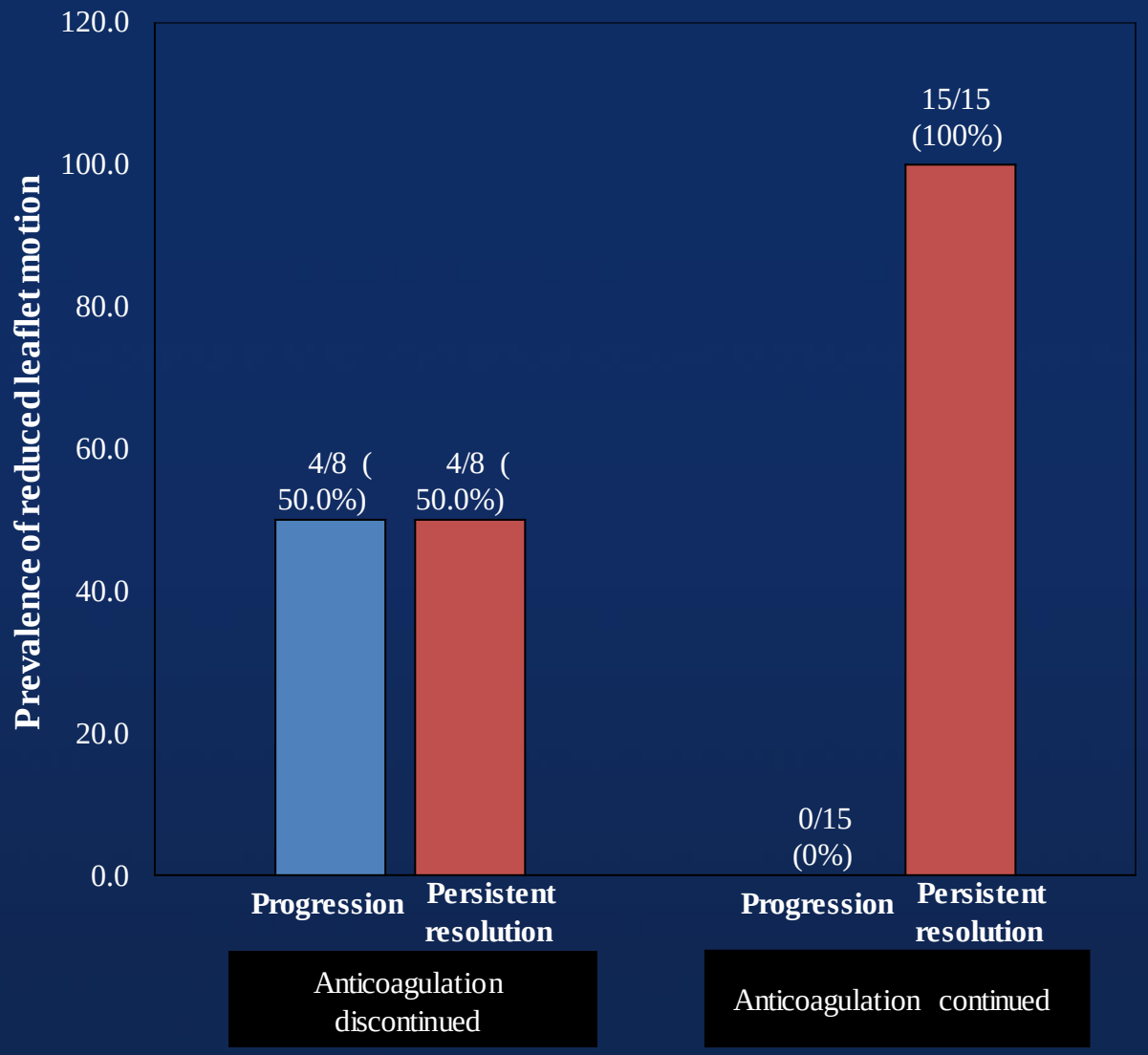



- **Resolution in 36 out of 36 patients** treated with anti coagulation (NO ACs, n=12; warf arin, n=24)
- **Persistence/progres sion in 20 out of 22 patients** not treated with anticoagulati on

**P<0.0001**

Chakravarty T, et al. Lancet 2017.

# Impact of Discontinuation of Anticoagulation Following Resolution of Reduced Leaflet Motion

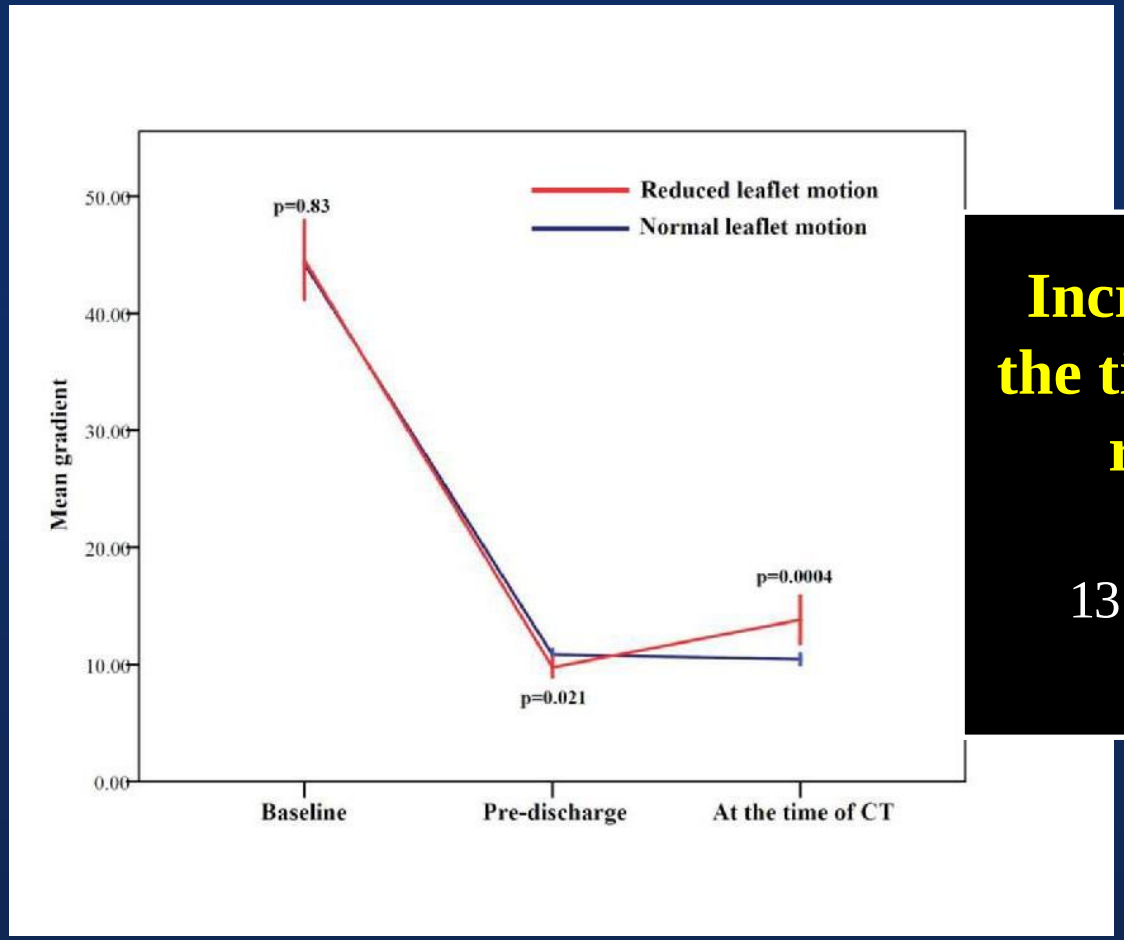



- Reduced leaflet motion **recurred in 4 out of 8 patients** in whom anticoagulation was discontinued
- Reduced leaflet motion **did not recur in the 15 patients** who were continued on anticoagulation

**P=0.008**

Chakravarty T, et al. Lancet 2017.

# Impact of Reduced Leaflet Motion on Valve Hemodynamics

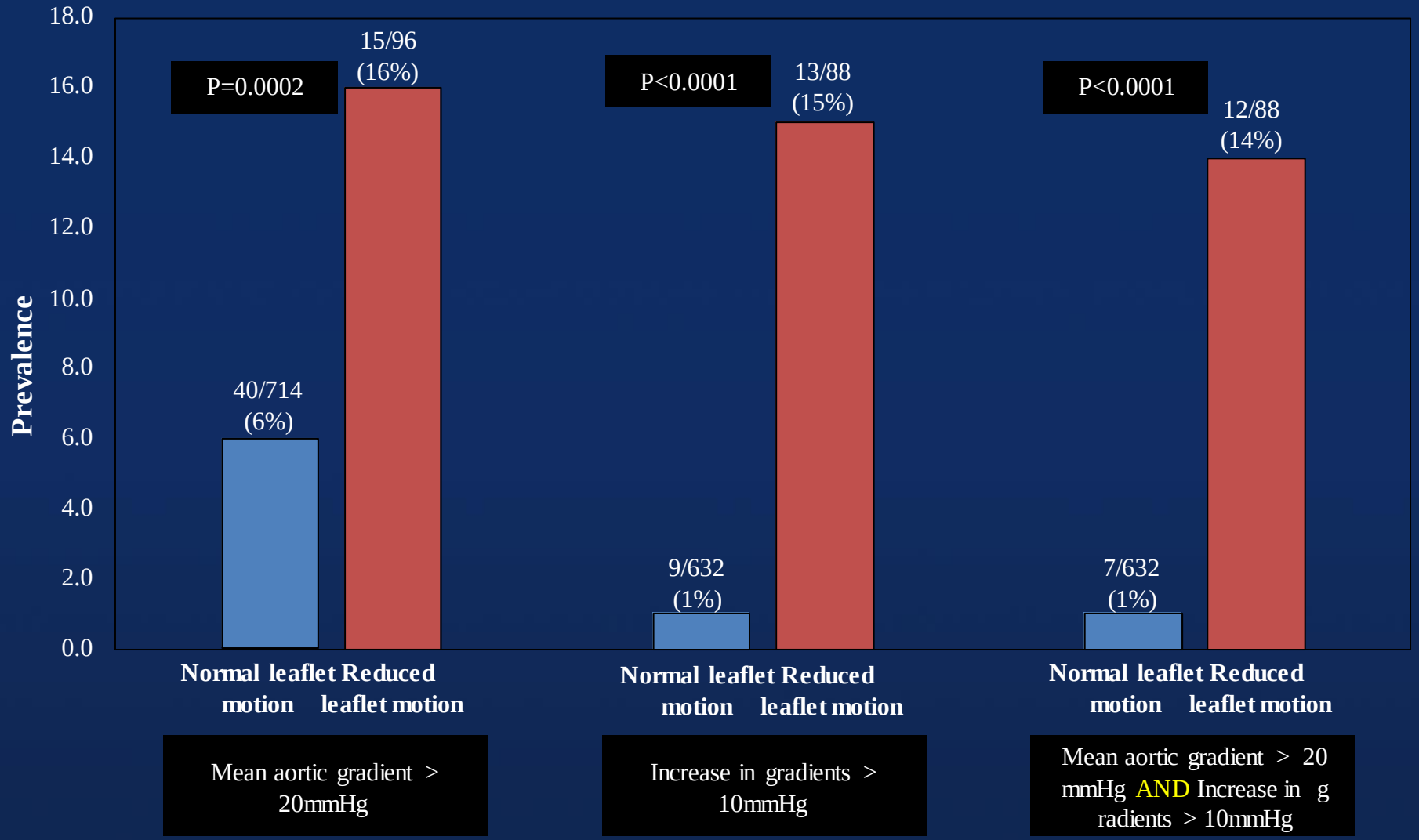



**Increased mean gradients at the time of CT in patients with reduced leaflet motion**

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 |

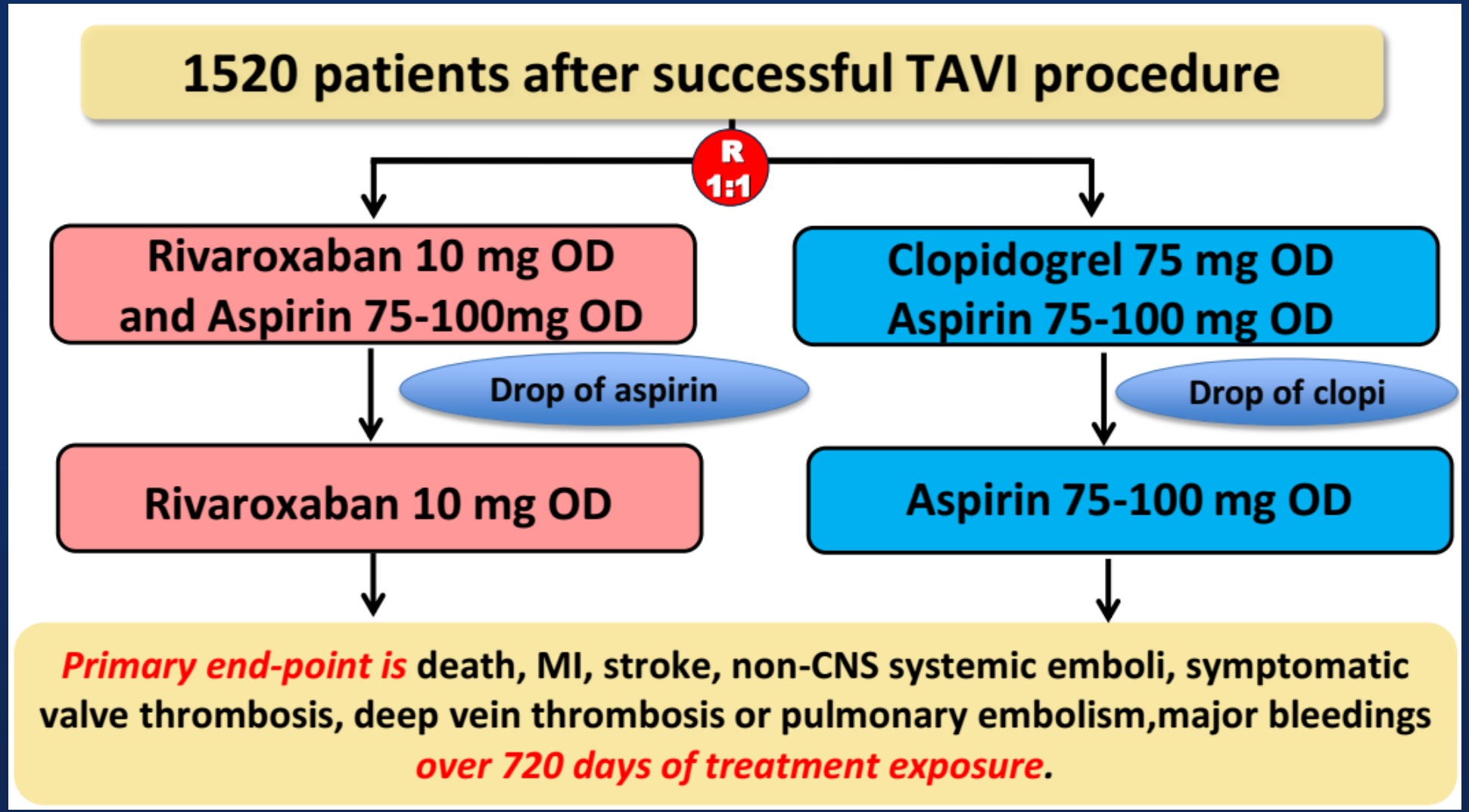
- No significant difference in strokes; but increased risk of TIAs and strokes/TIAs
- TIA=Transient ischemic attack/ * All strokes include hemorrhagic and ischemic strokes



Chakravarty T, et al. Lancet 2017.

# Rivaroxaban vs. DAPT after TAVR

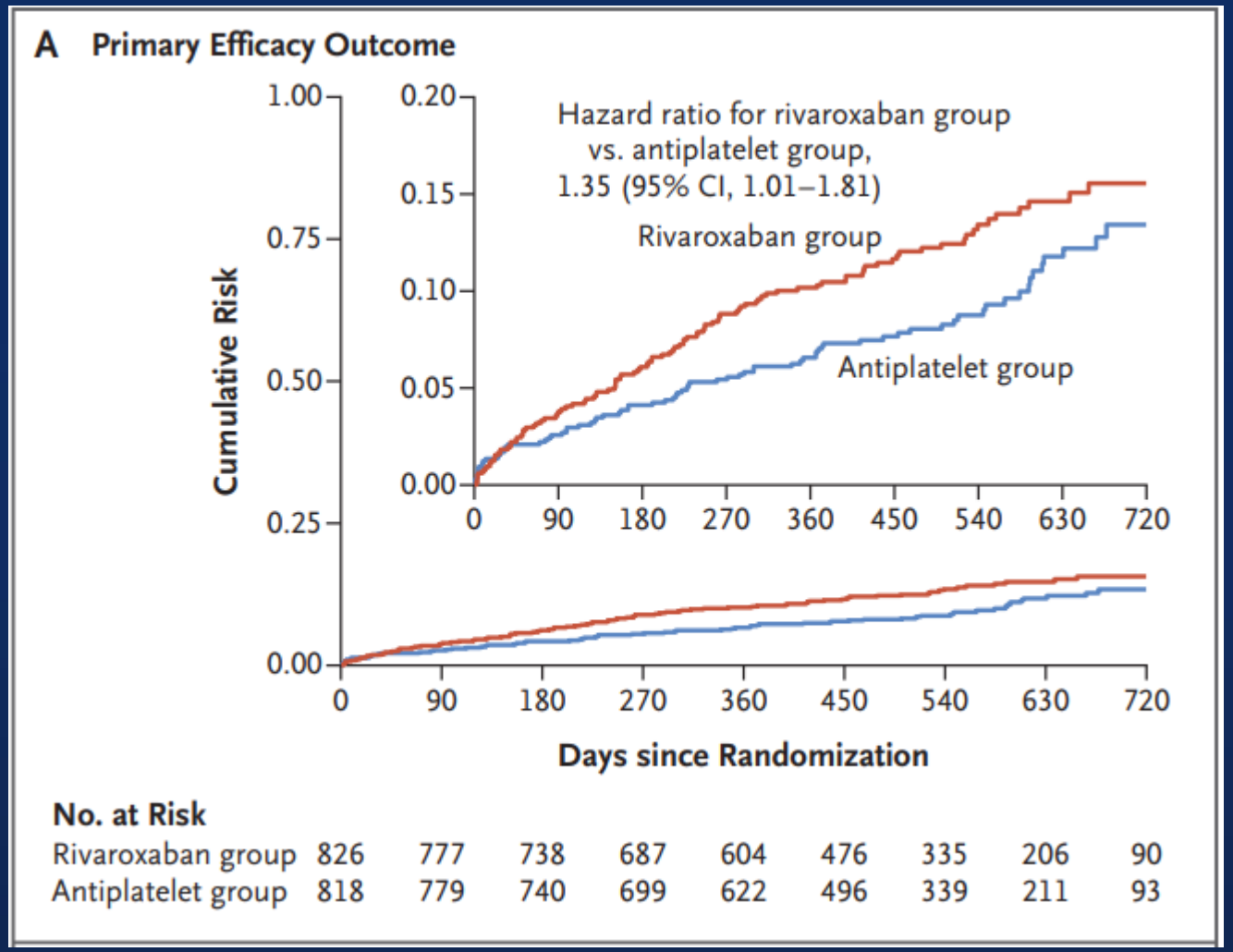
## GALILEO Study




Stephan Windecker et al. Am Heart J 2017.

# Rivaroxaban vs. DAPT after TAVR

## GALILEO Study




**Primary Efficacy Outcomes**

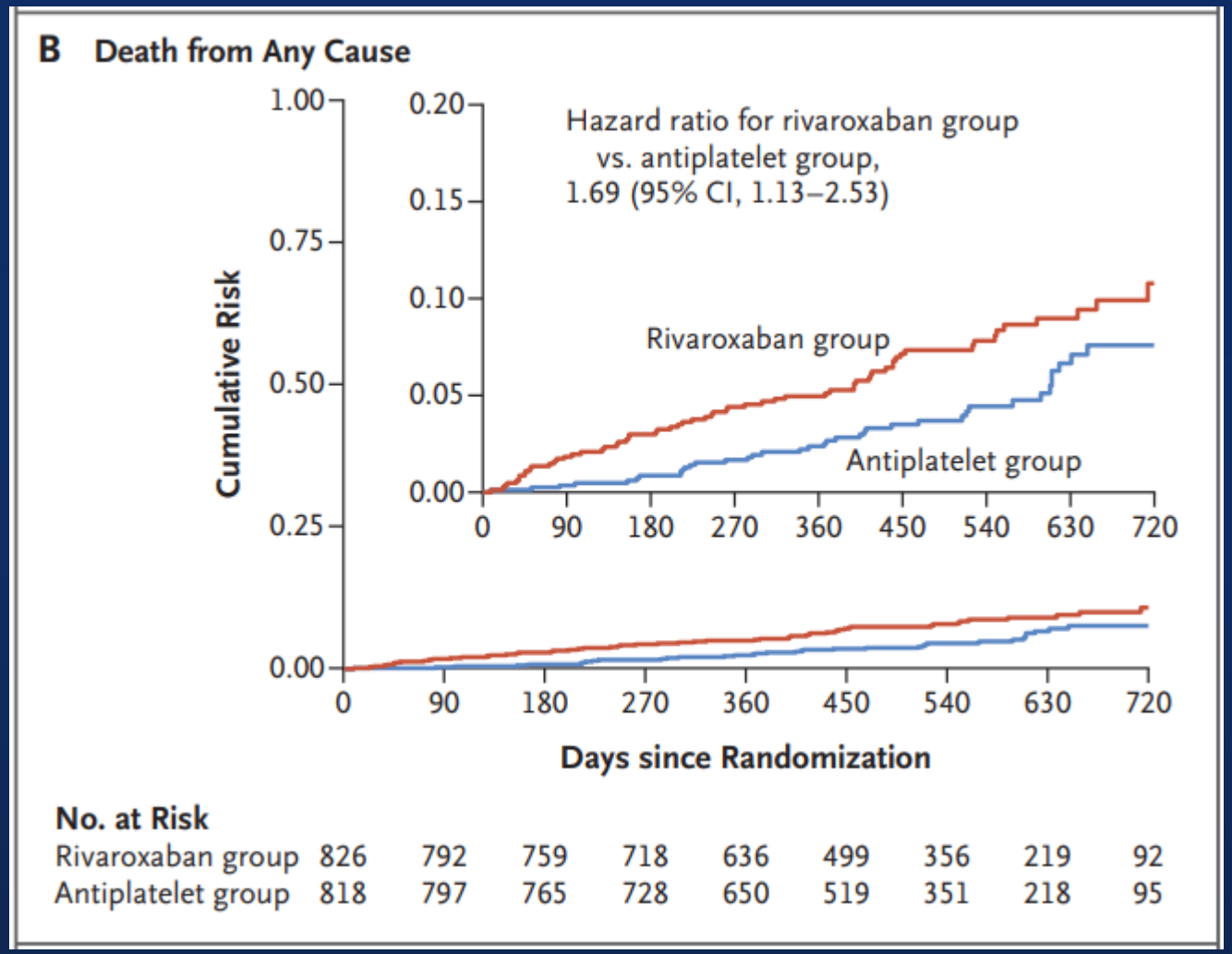
Death, stroke, MI, symptomatic valve thrombosis, PTE, DVT, systemic embolism



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

# Rivaroxaban vs. DAPT after TAVR

## GALILEO Study

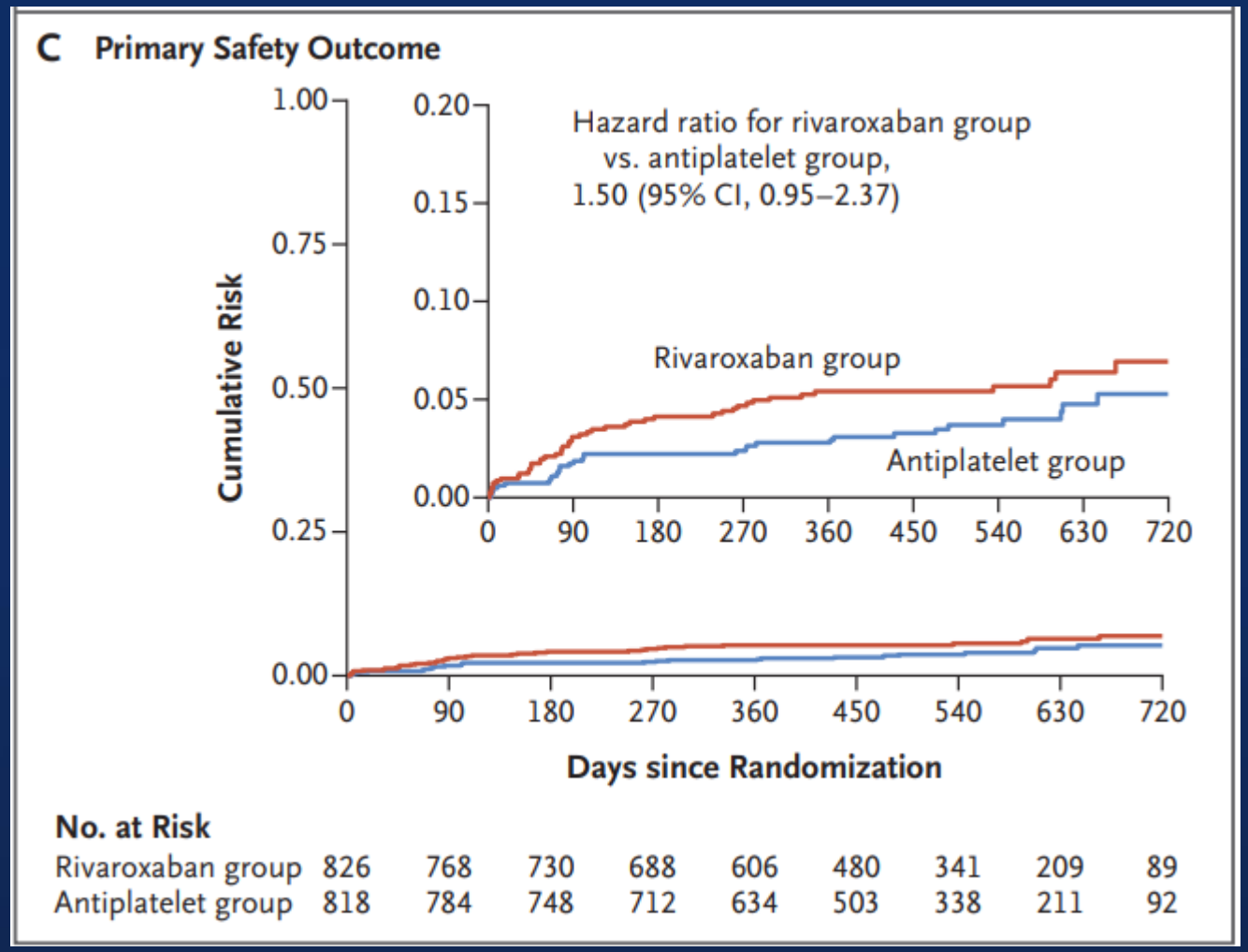





G.D. Dangas et al. N Engl J Med 2020;382:120-9

# Rivaroxaban vs. DAPT after TAVR

## GALILEO Study




**Primary Safety Outcomes**

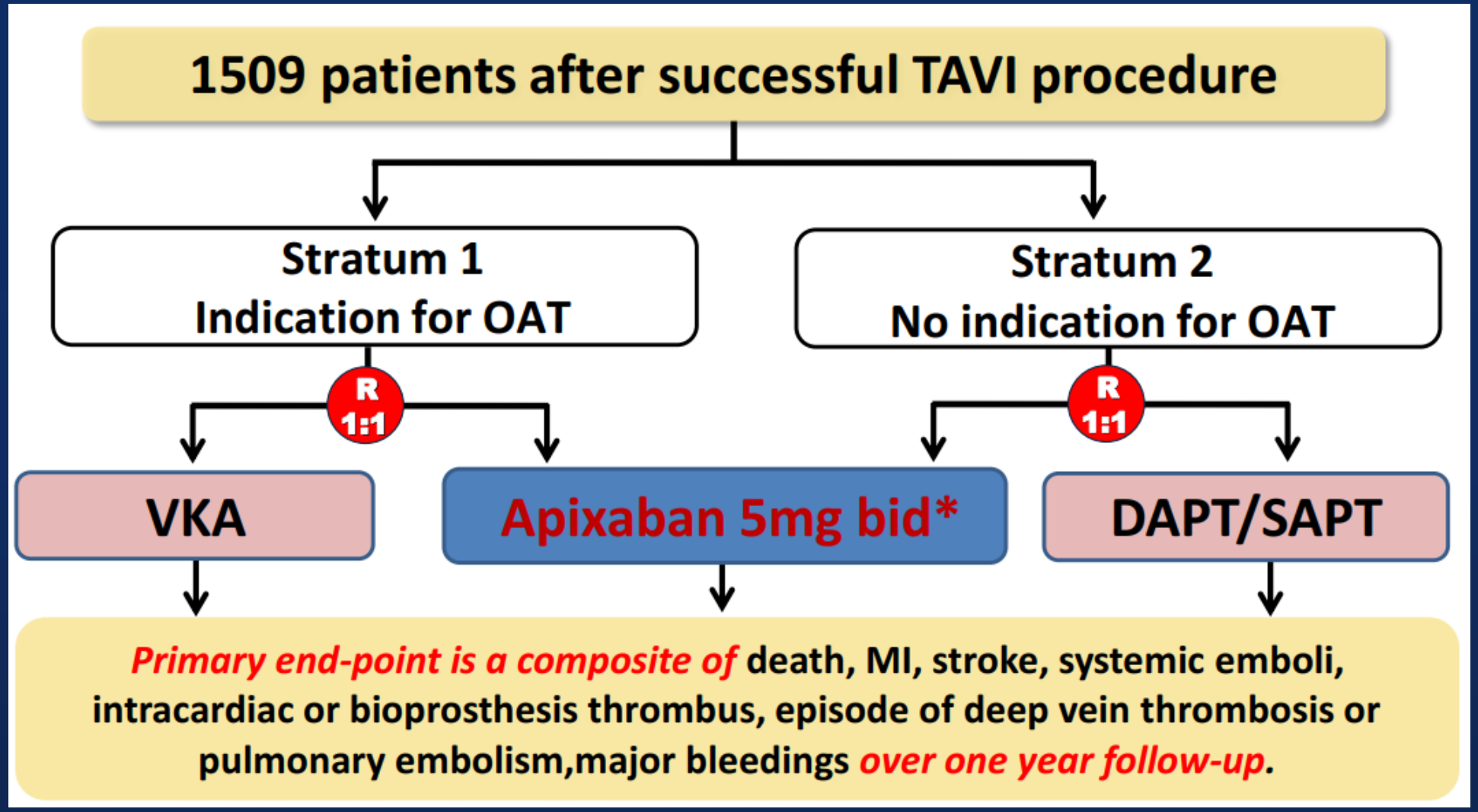
VARC life-threatening, disabling, or major bleeding



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

# Apixaban vs. VKA vs. DAPT after TAVR

## ATLANTIS Study





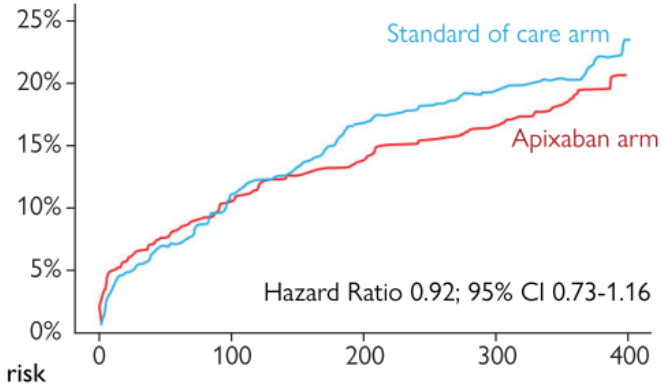

Jean-Philippe Collet et al. Am Heart J 2018.

# 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



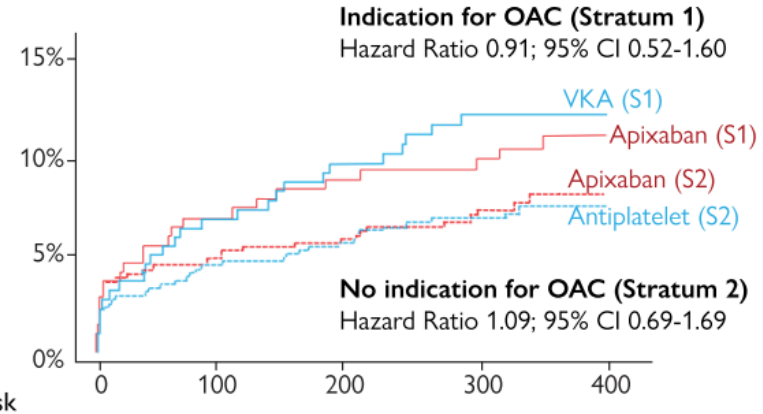

| No at risk | | | | | |
|---|---|---|---|---|---|
| SOC | 751 | 646 | 583 | 555 | 42 |
| Apixaban | 749 | 645 | 612 | 585 | 27 |

| | Apixaban (n= 749) | Standard-of-care (n= 751) | $P_{ist}$ | 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)



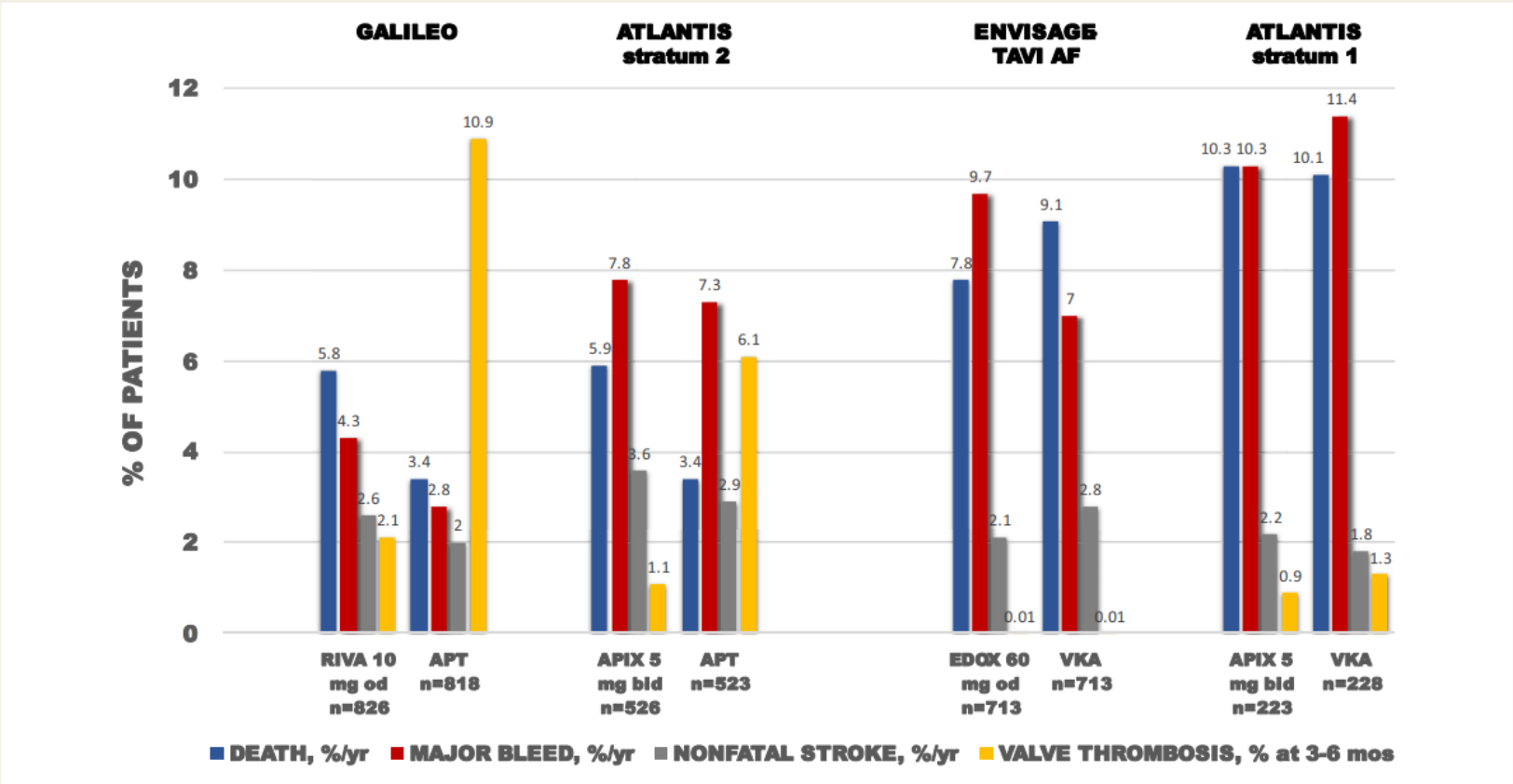

| No at risk | | | | | |
|---|---|---|---|---|---|
| VKA (S1) | 228 | 196 | 180 | 170 | 14 |
| Apixaban (S1) | 223 | 188 | 177 | 167 | 10 |
| Antiplat(S2) | 526 | 479 | 459 | 441 | 18 |
| Apixaban (S2) | 523 | 480 | 457 | 441 | 31 |

| | 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

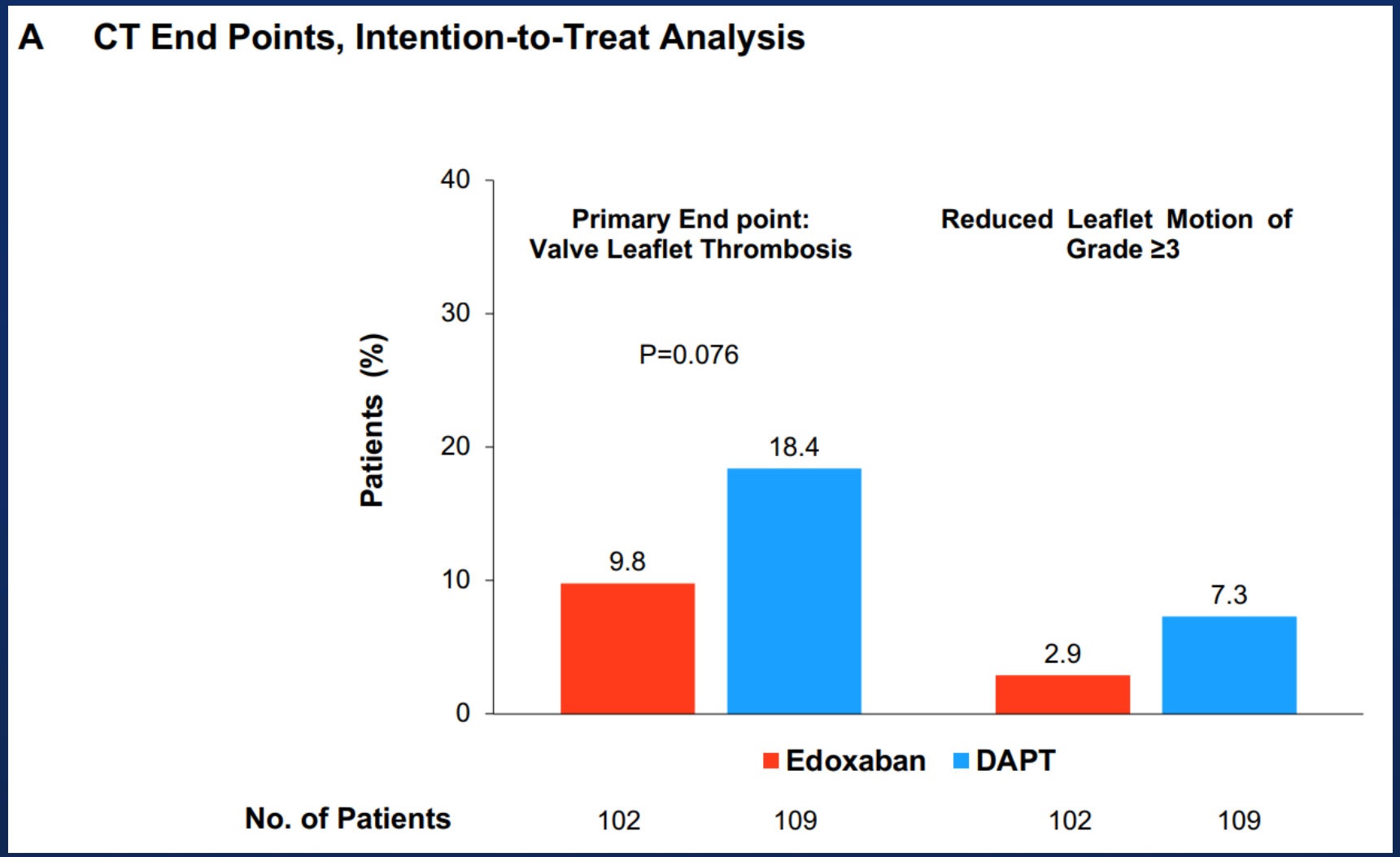
- Follow-up MRI imaging will be matched with immediate post-TAVR scans, and subtraction analyses are performed to identify new lesions in the entire brain. MRI outcomes included calculation of number and volume of new DWIs (postprocedure – 6 months) by subtraction of the existing baseline lesions in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

# Neurological and neurocognitive function assessment

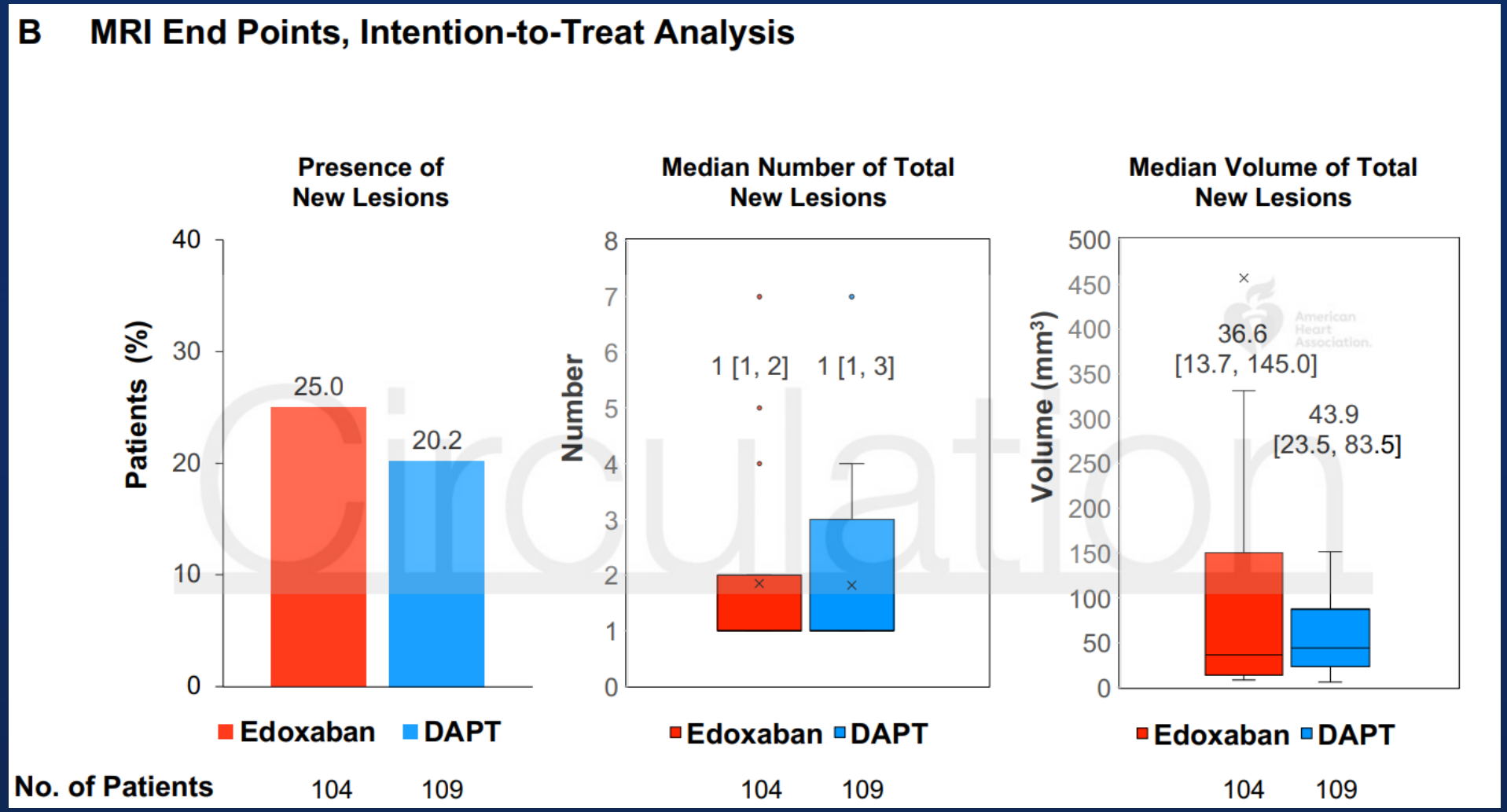
- All study subjects will undergo detailed neurologic and cognitive assessment at 1-7 days (baseline) and 6 months post-TAVR procedure

- 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).

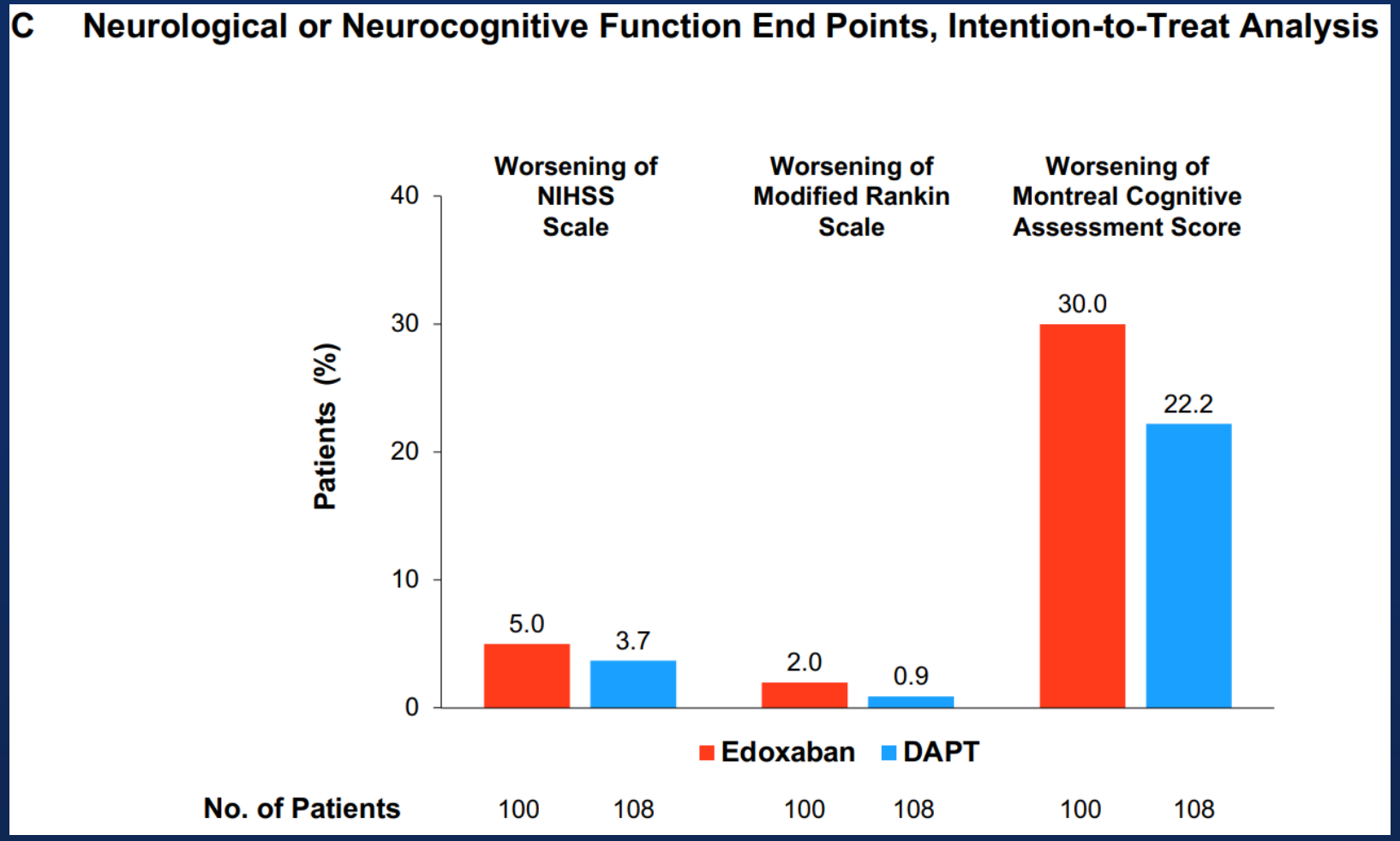
# CT End Points



# MRI End Points

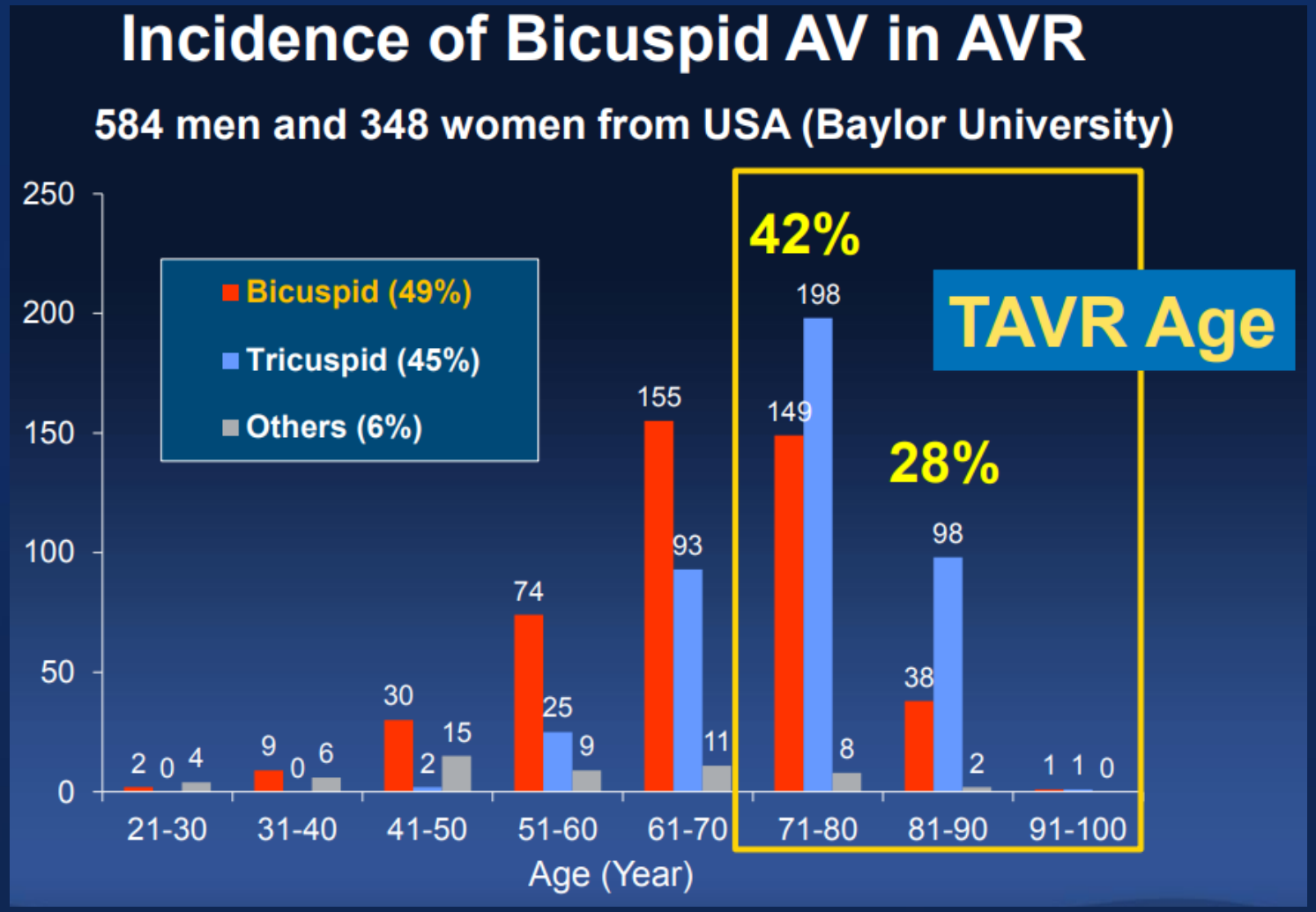


# Neurological or Neurocognitive Function End Points



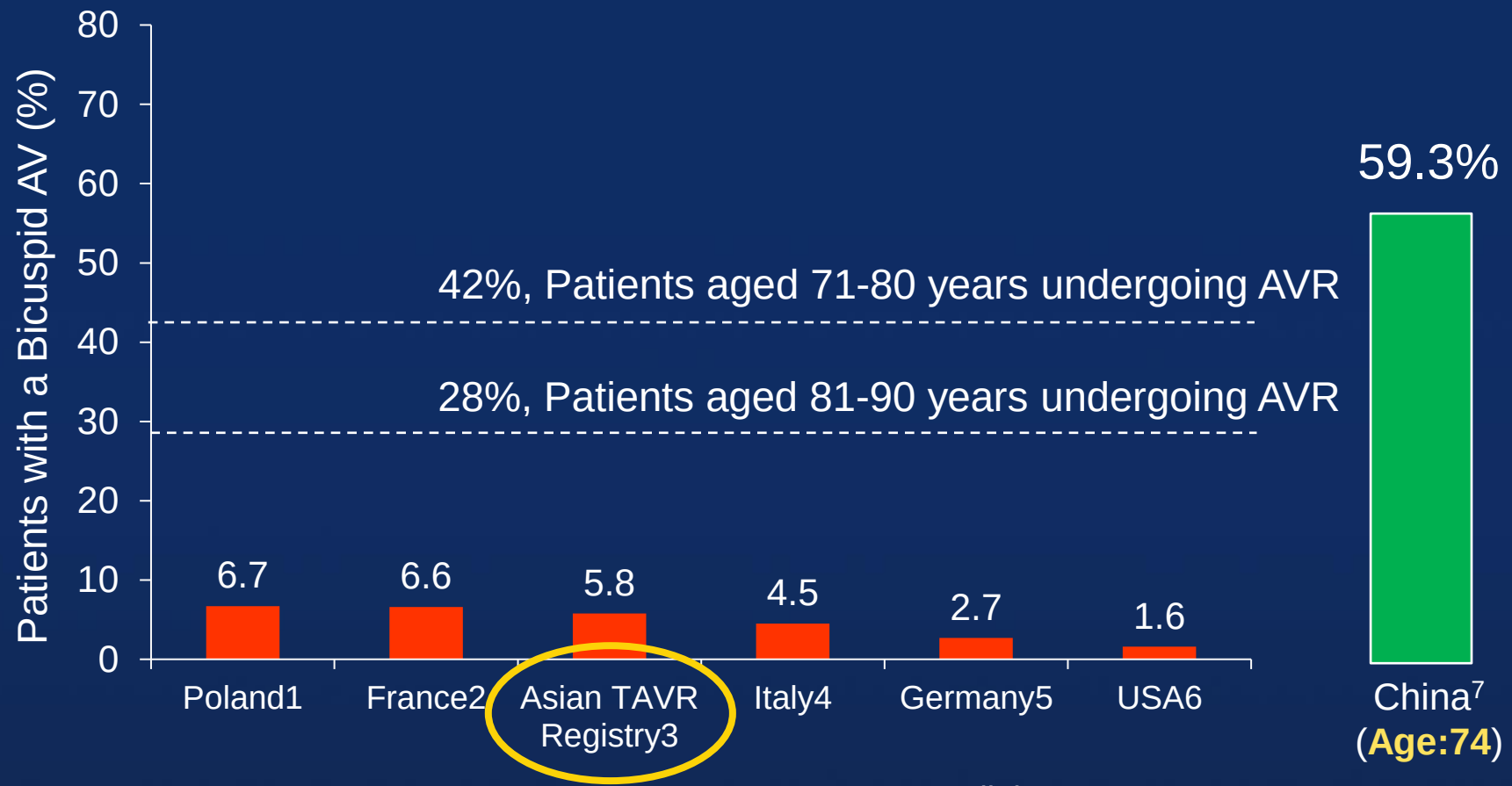
# Bicuspid aortic valve

# 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

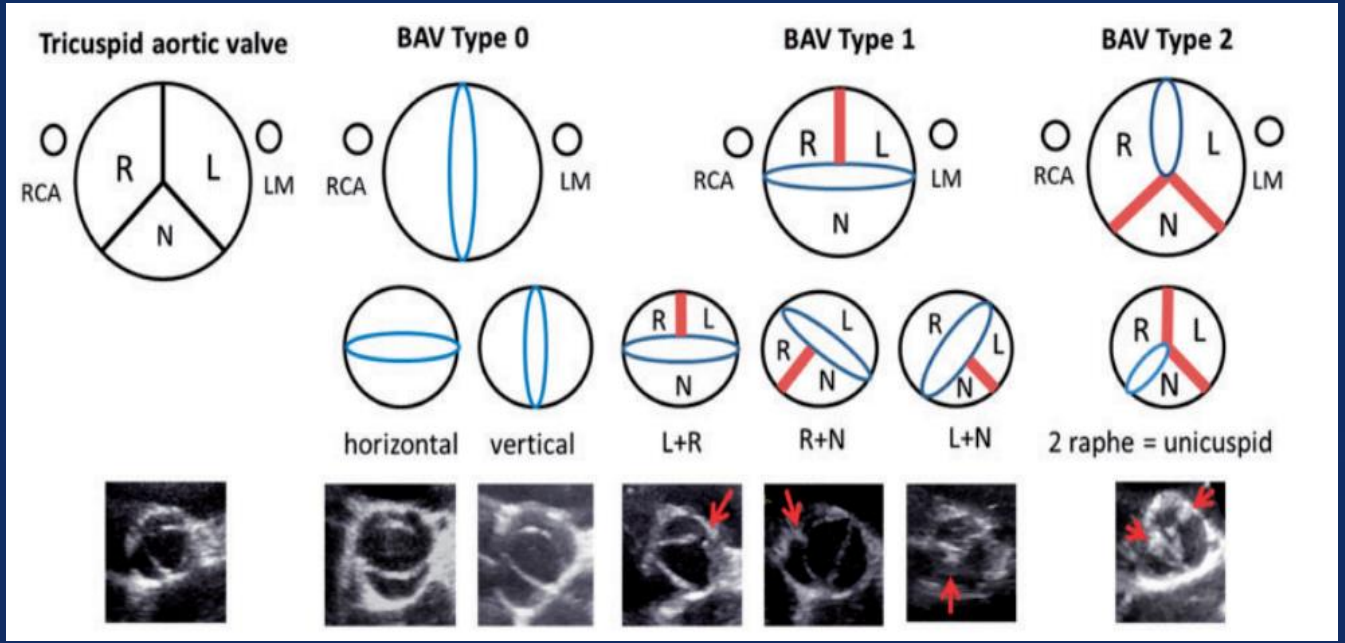
## Procedural

- 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

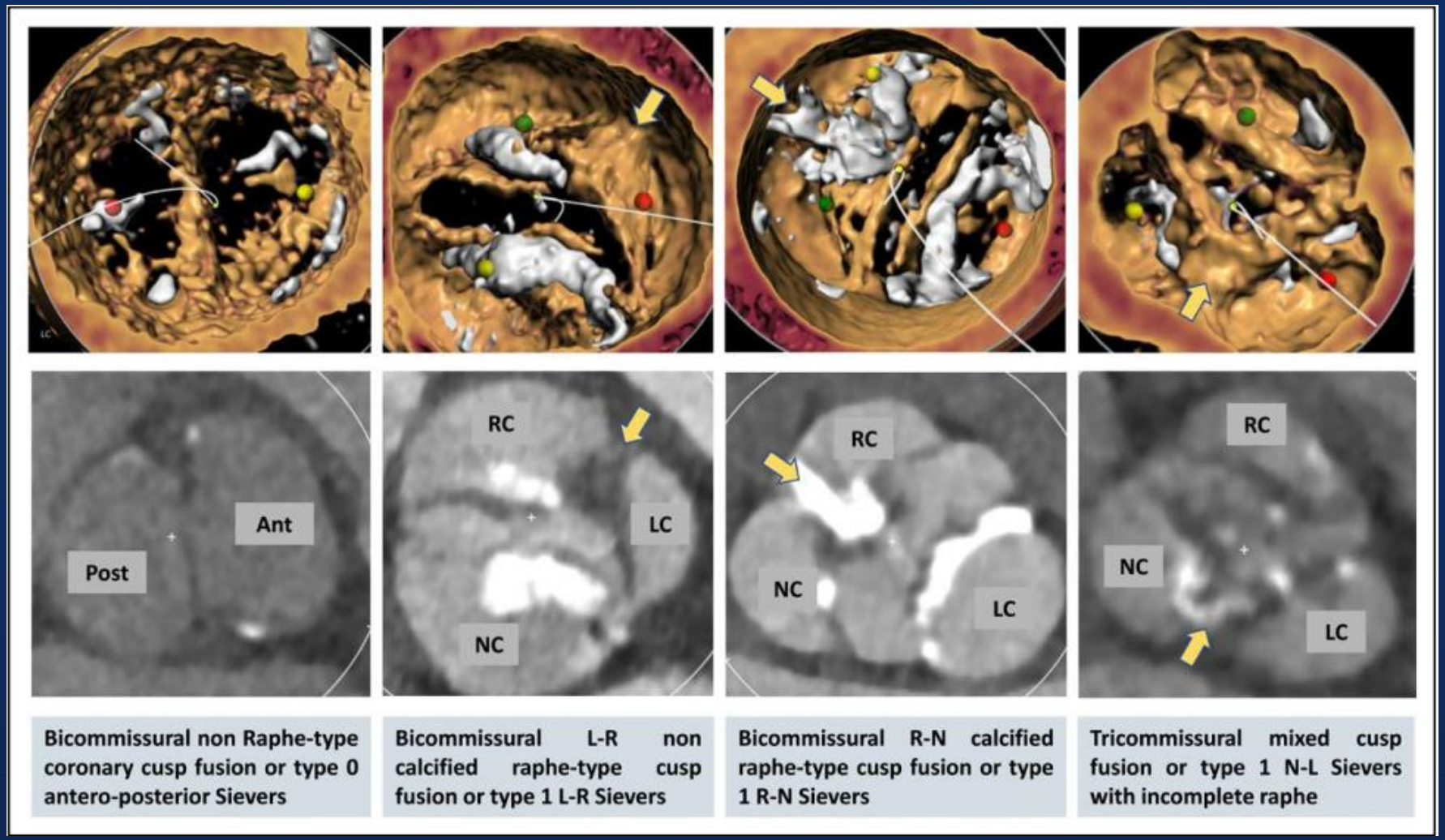



## Inter-ethnic differences in BAV

| | 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

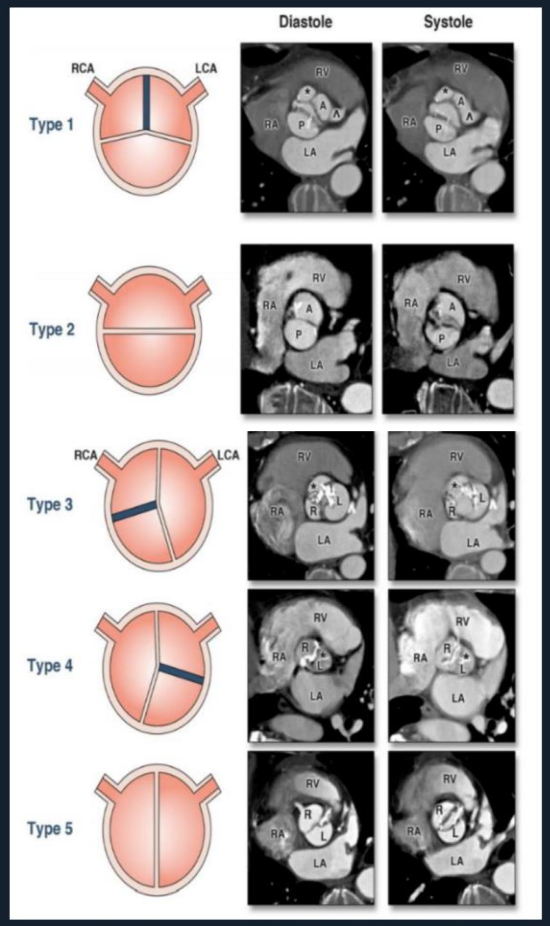




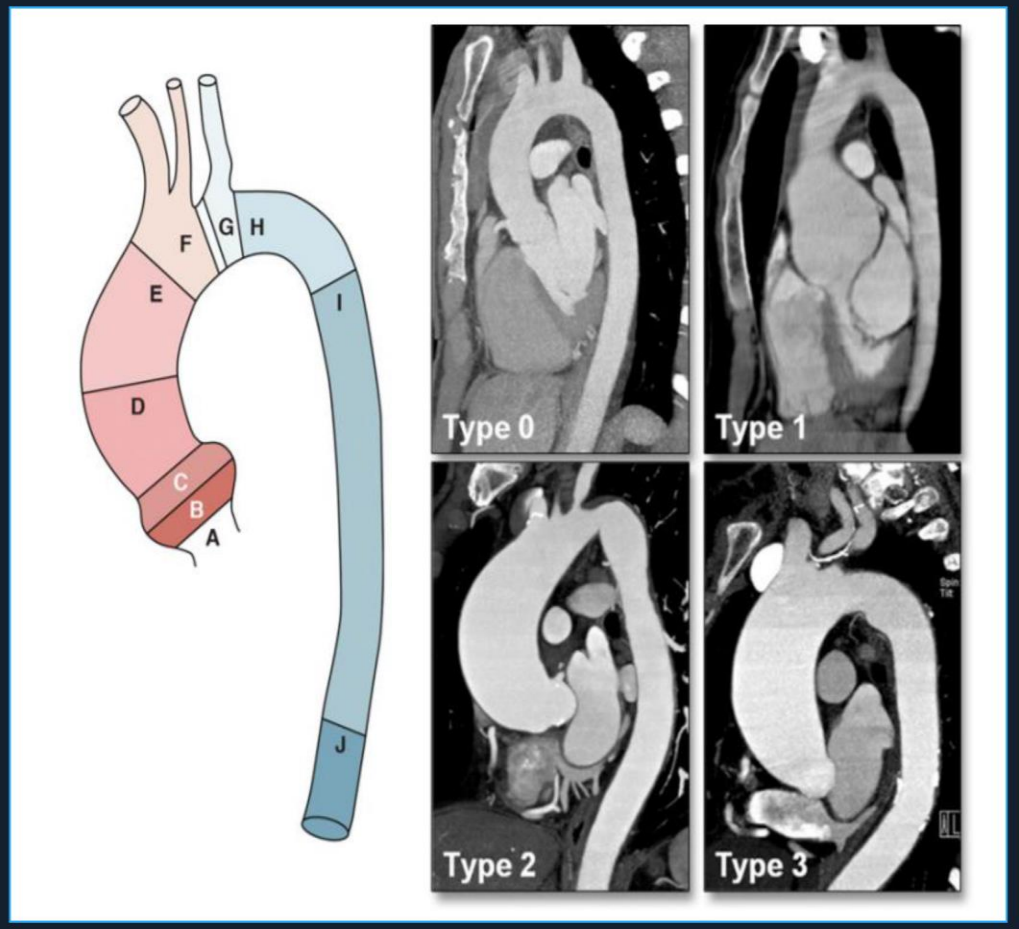

Flvien Vincent et al. Circulation 2021;143:1043-1061

# Spectrum of BAV Disease

## Aortic Valve Morphology

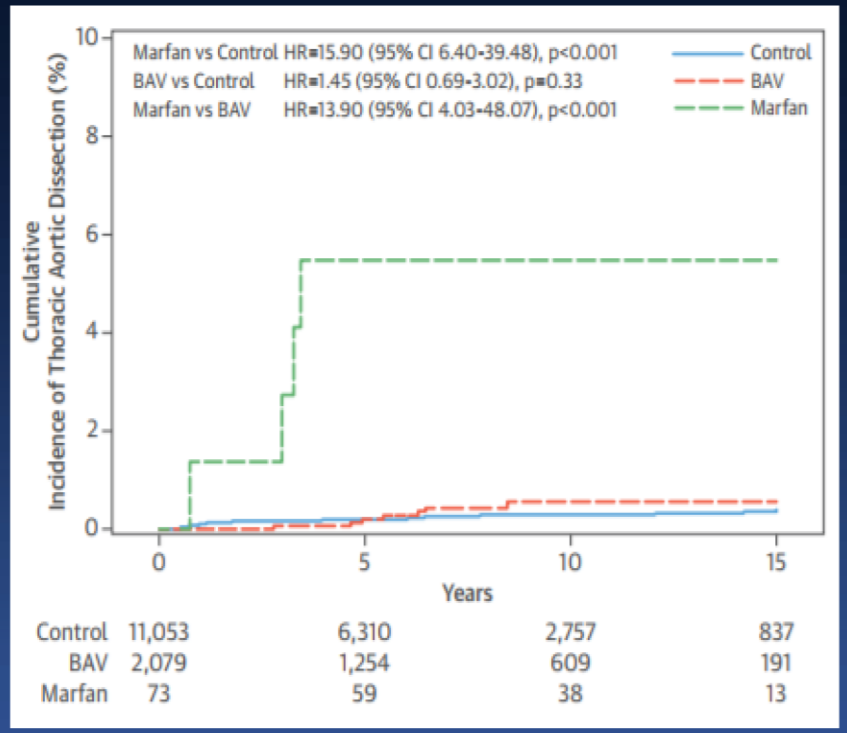



## Combined Aortopathy



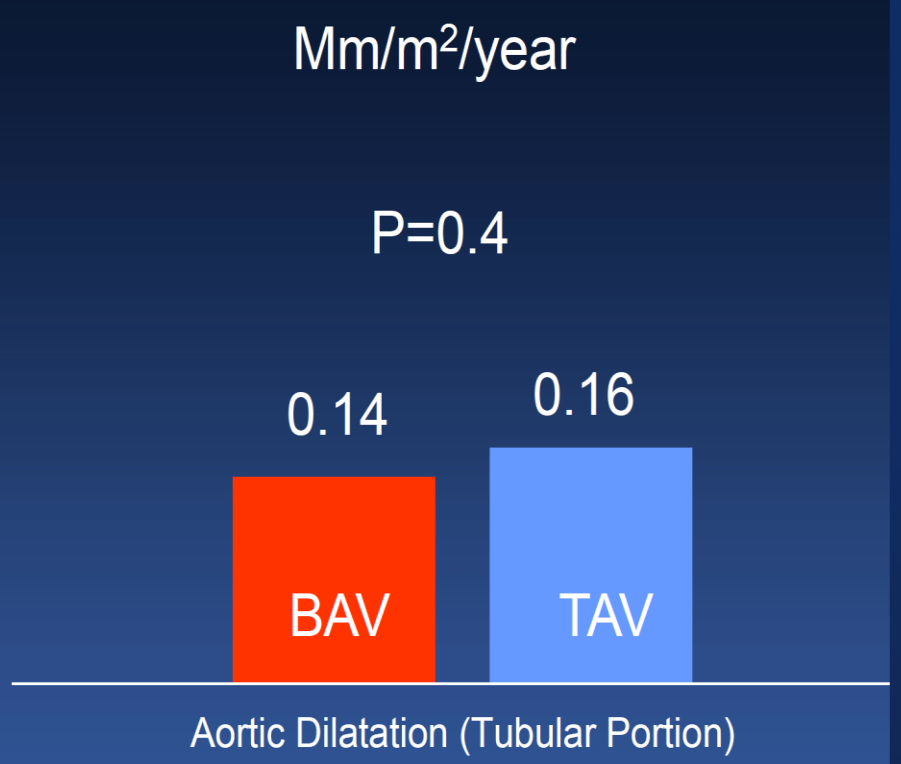
# BAV Aortopathy

## Risk Aortic Dissection After SAVR



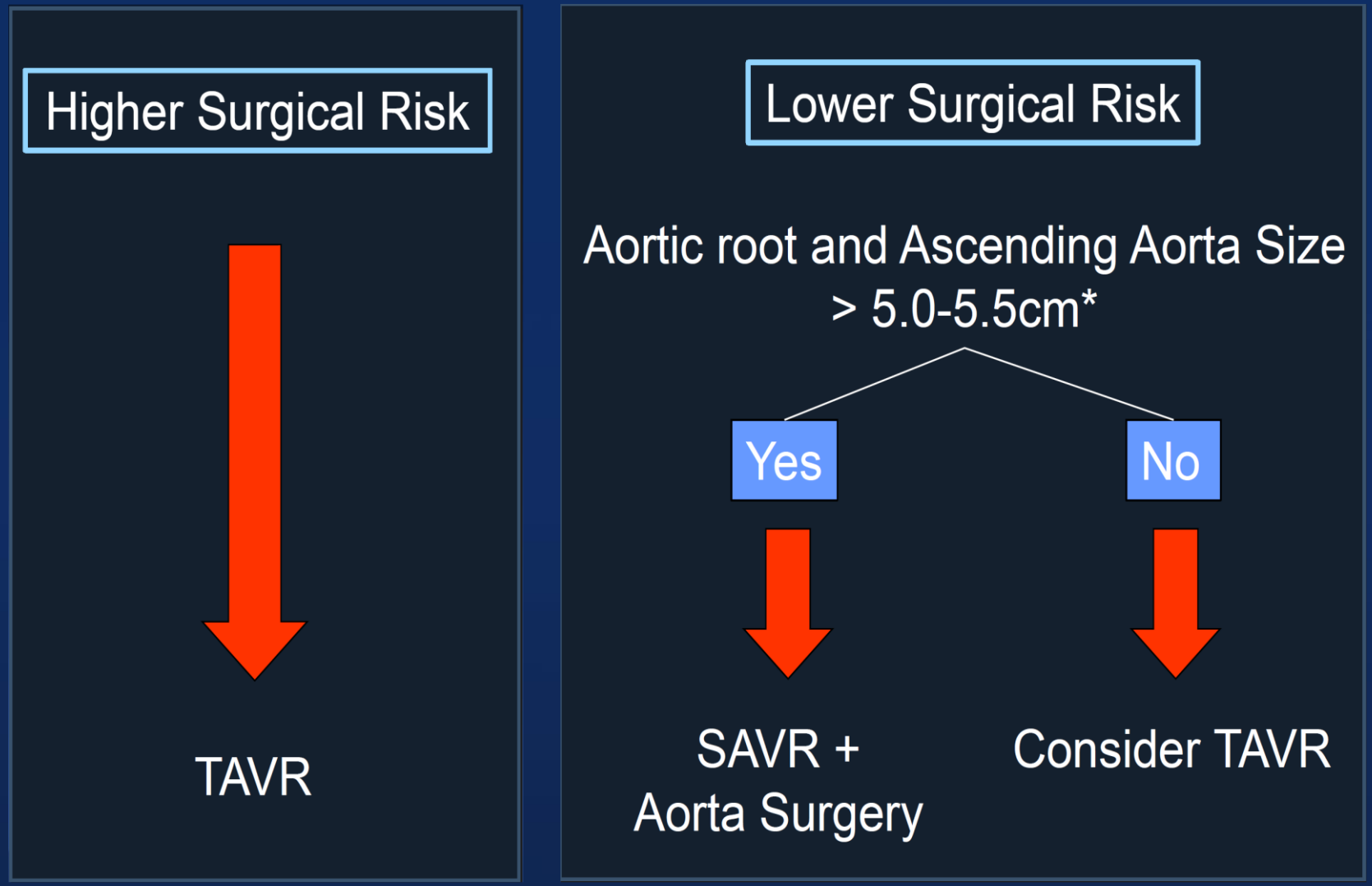

Itagaki S et al. JACC 2015 Jun 9;65(22):2363-9

## Rate of Ao Dilatation After SAVR



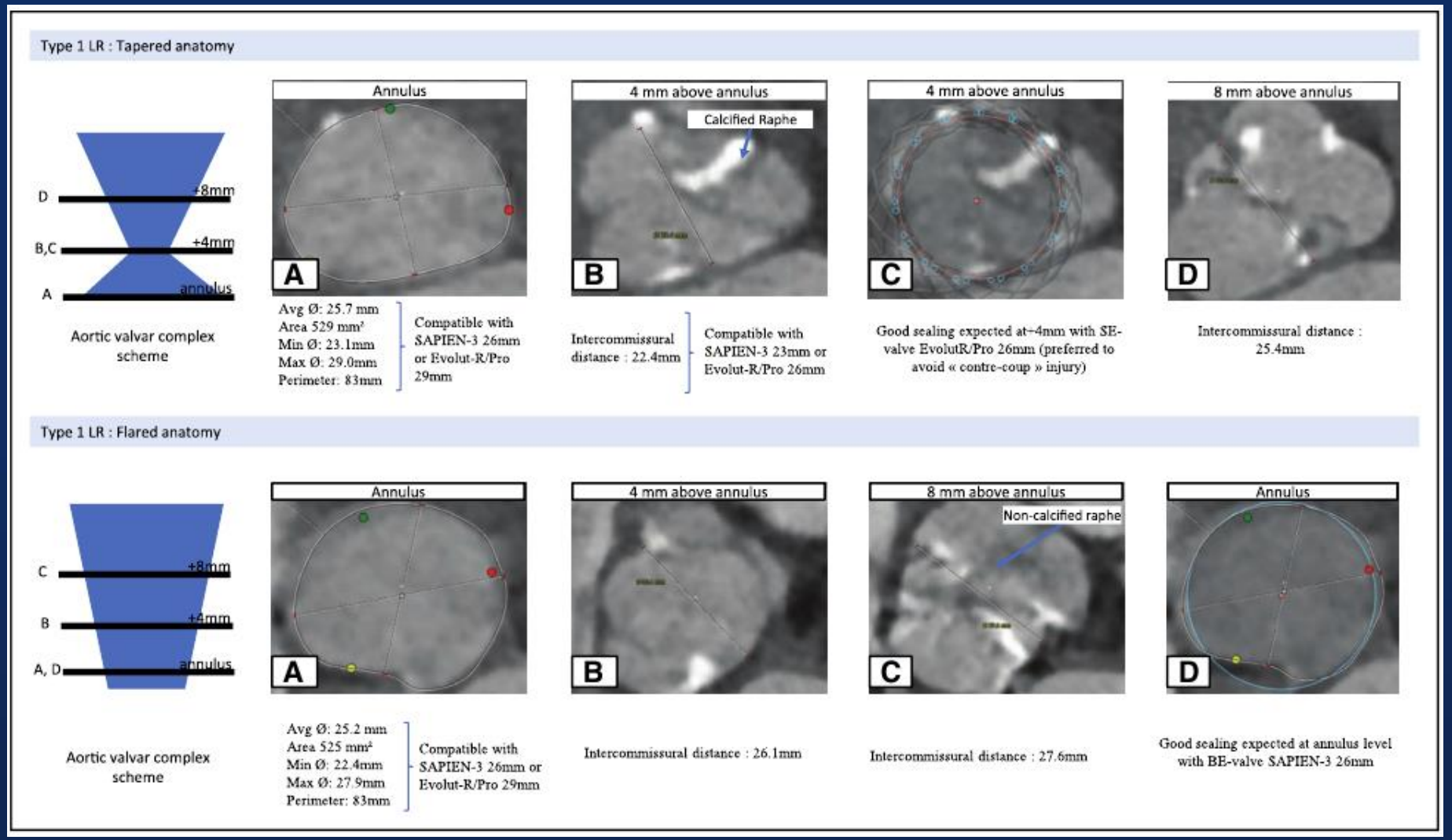

Kim YG et al. 2012 Dec;98(24):1822-7

# 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 |

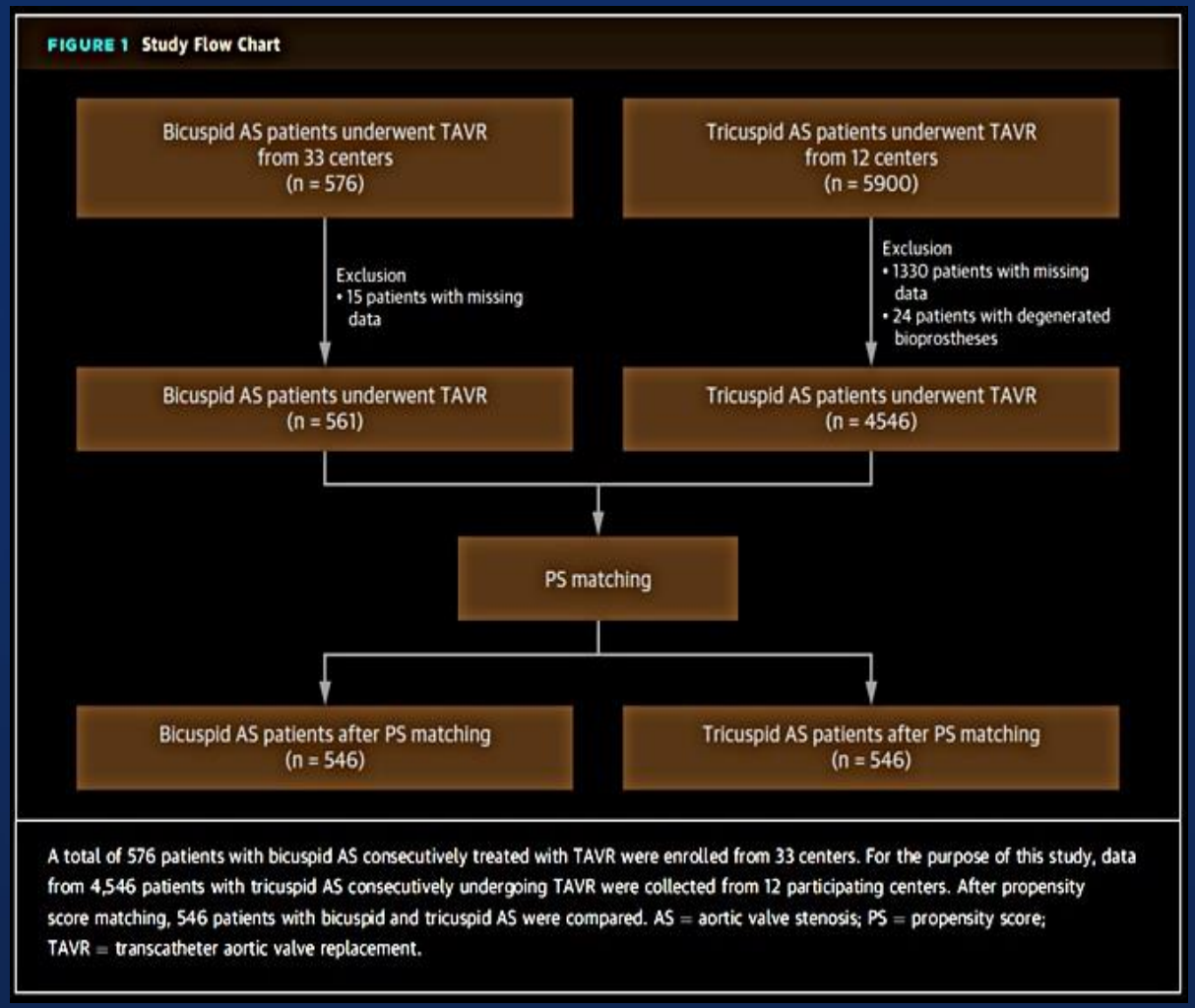

Bauer T et al. Am J Cardiol. 2014 ;113:518-21
Kochman et al. Am J Cardiol. 2014;114:757-62
Yousef et al. Int J Cardiol 2015;189:282-8
Mylotte al. J Am Coll Cardiol 2014 ;64:2330
Jilaihawi et al. JACC:Cardiovascular Imaging 2016;9:1145-58

# 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*

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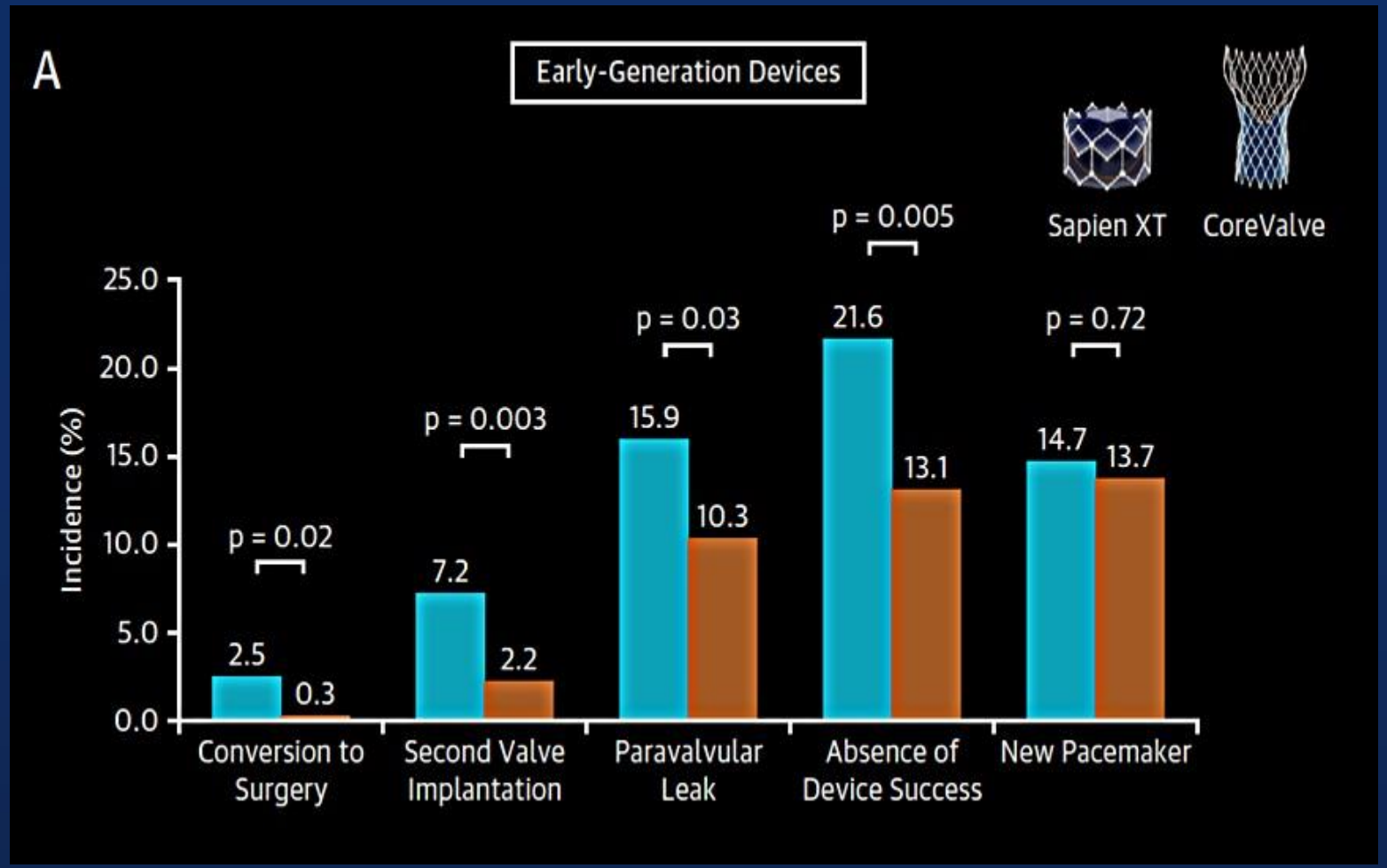




SH Yoon et al. JACC 2017;69:2579-89

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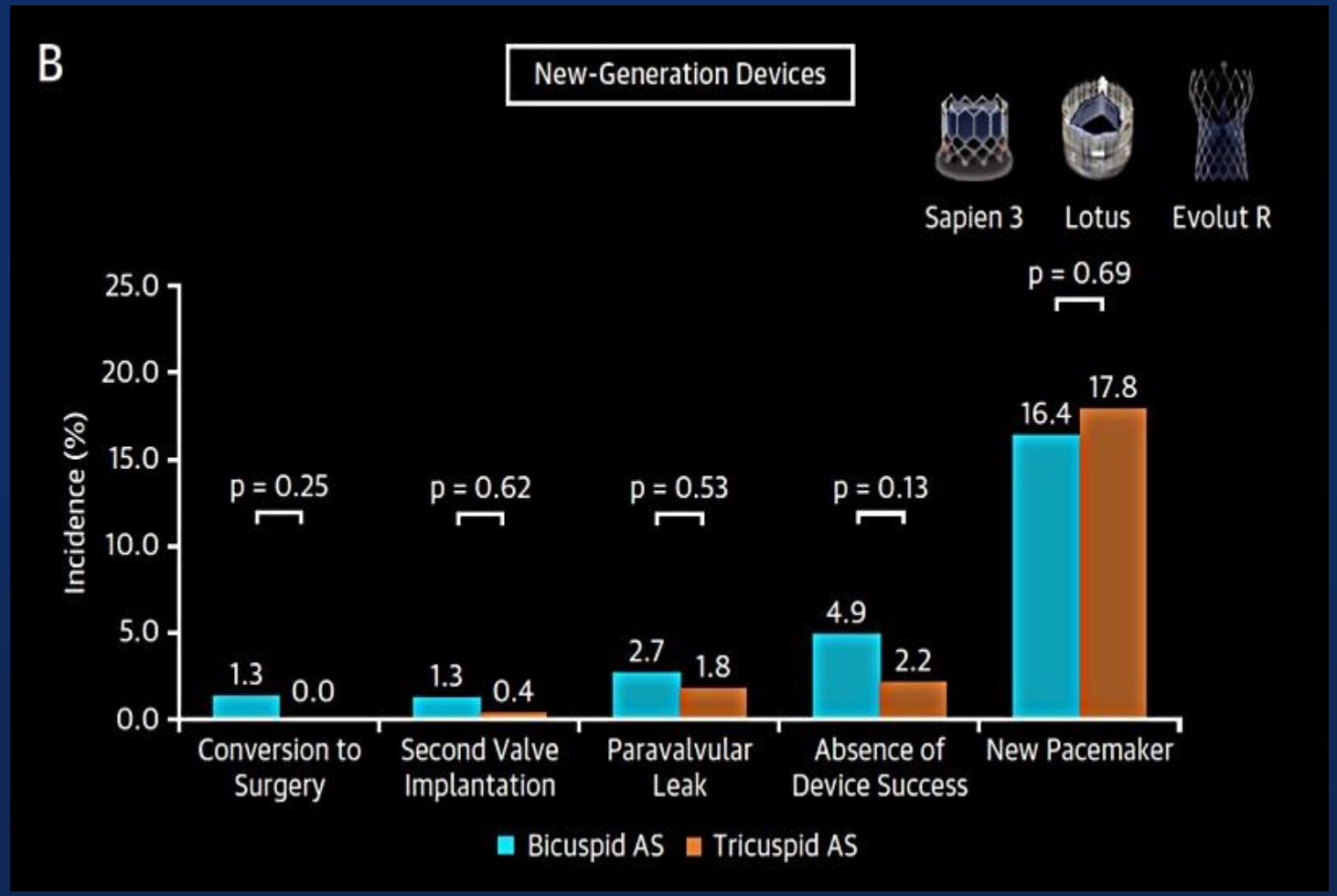
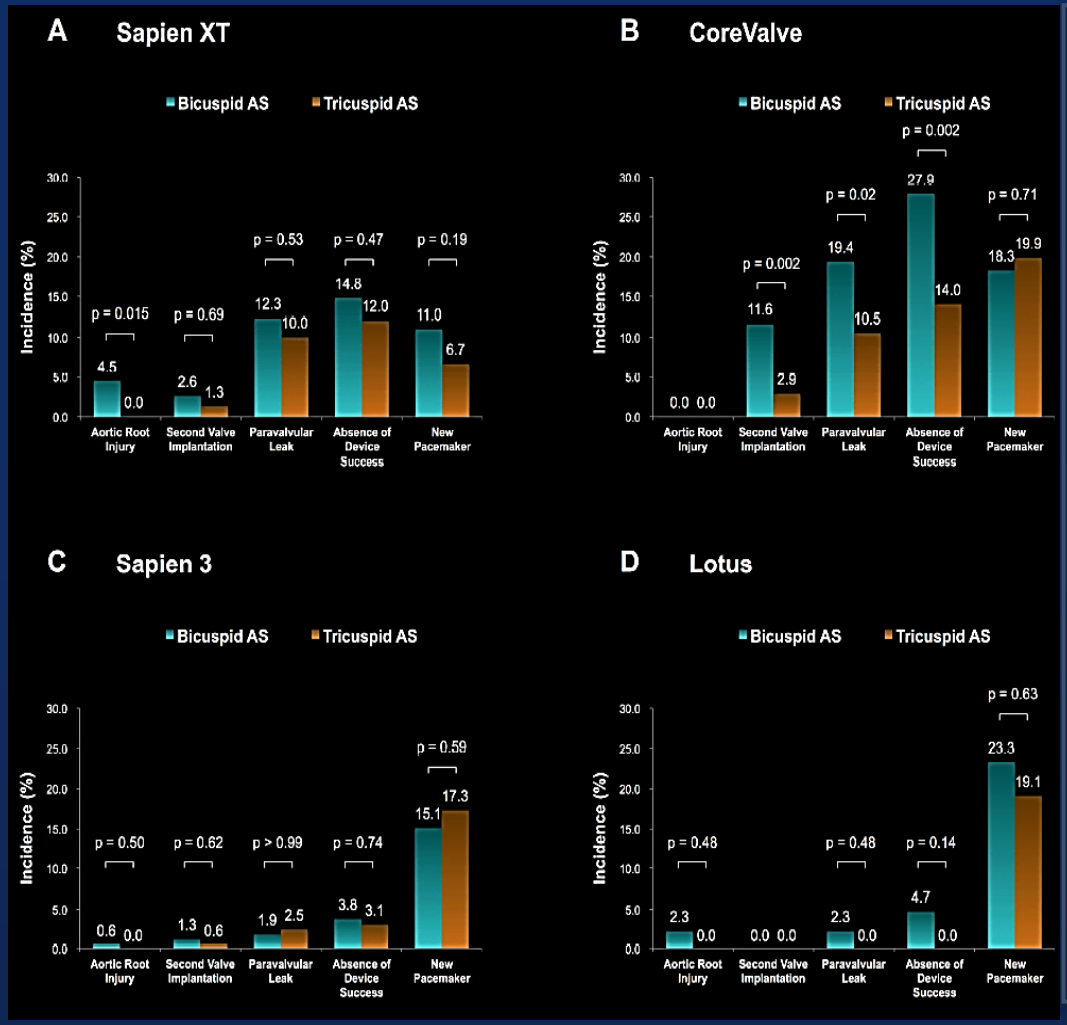





SH Yoon et al. JACC 2017;69:2579-89

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

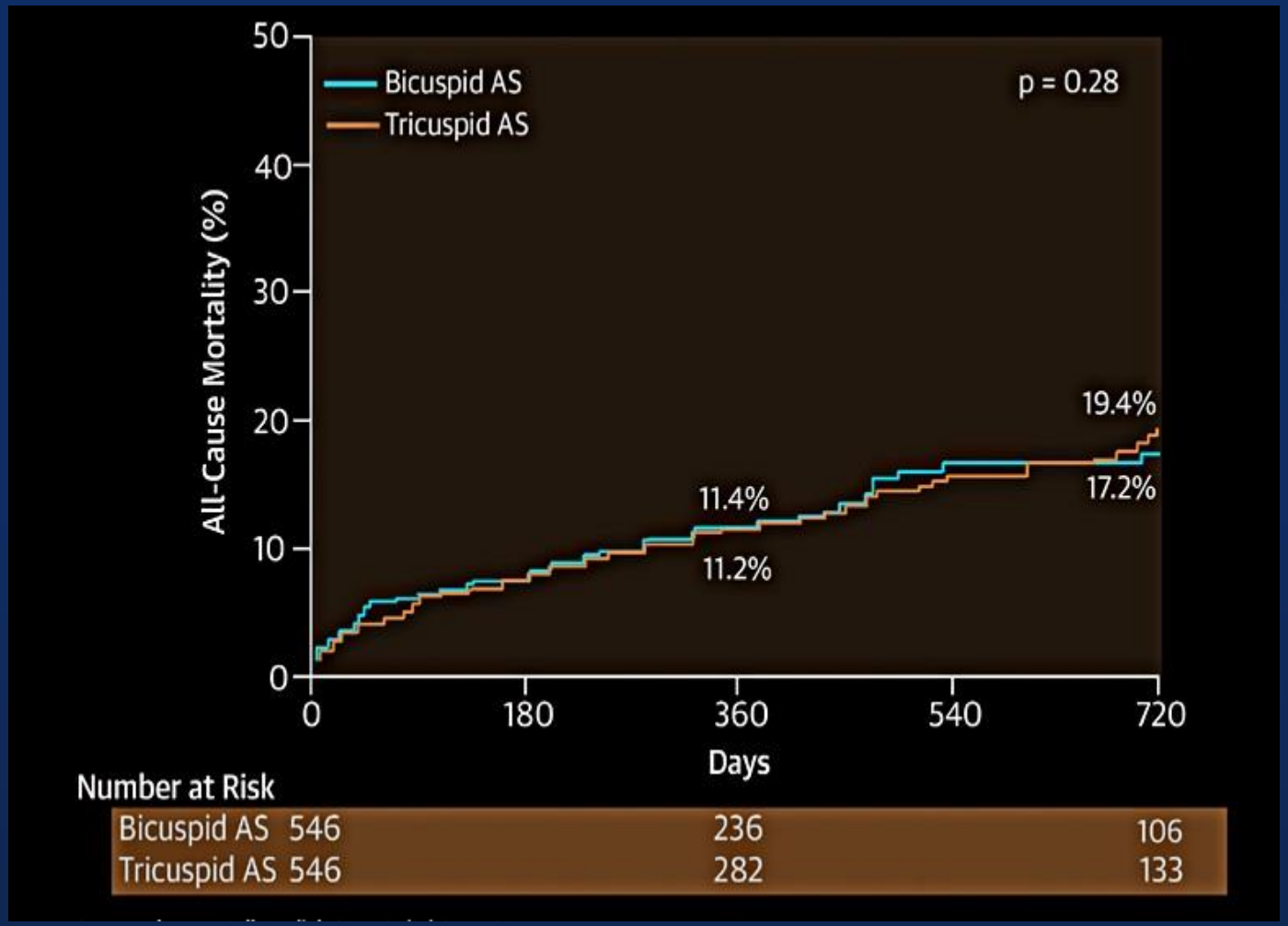



Within the group receiving early generation devices, bicuspid AS had more frequent

- 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]

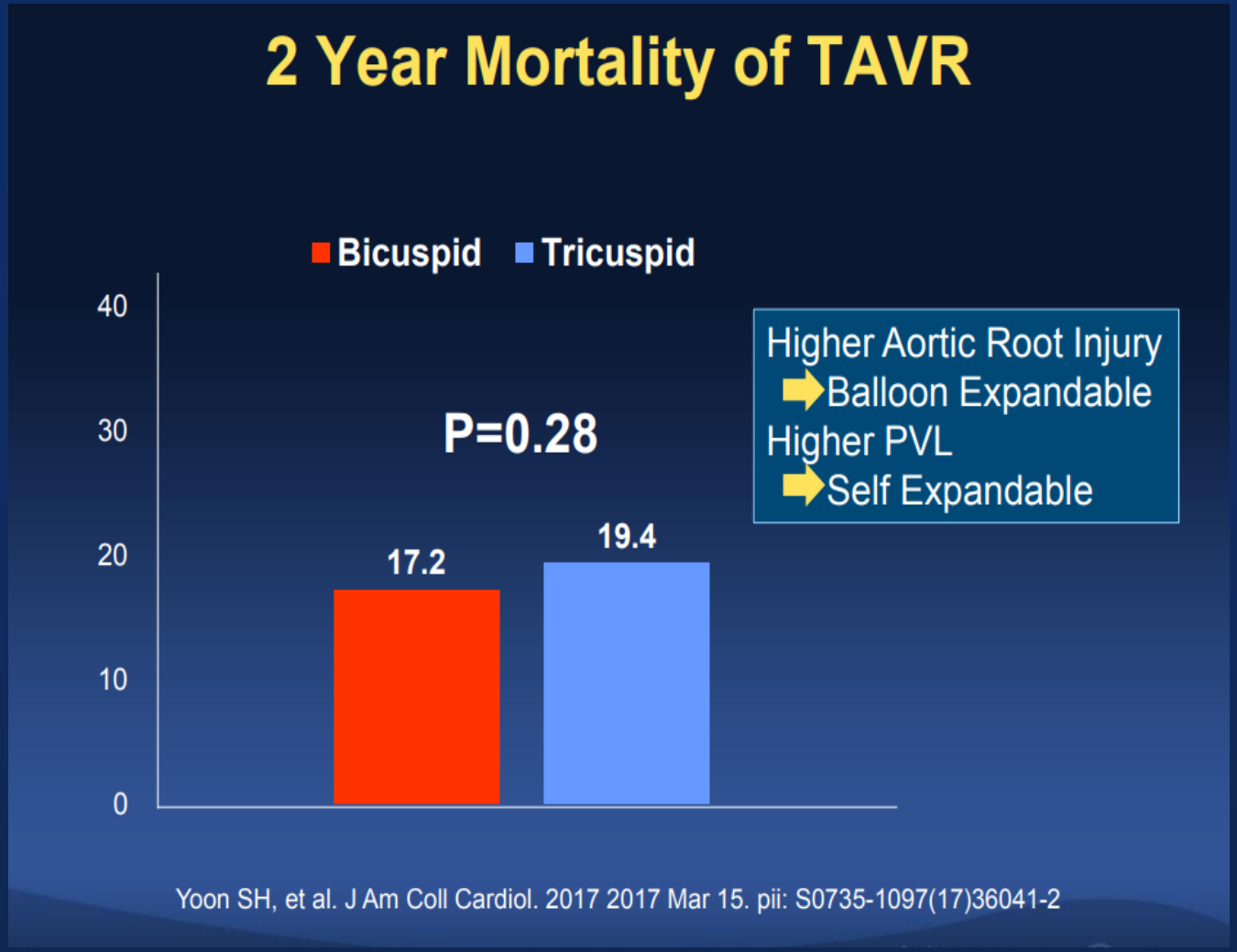
# 2-year outcomes of Bicuspid vs. Tricuspid



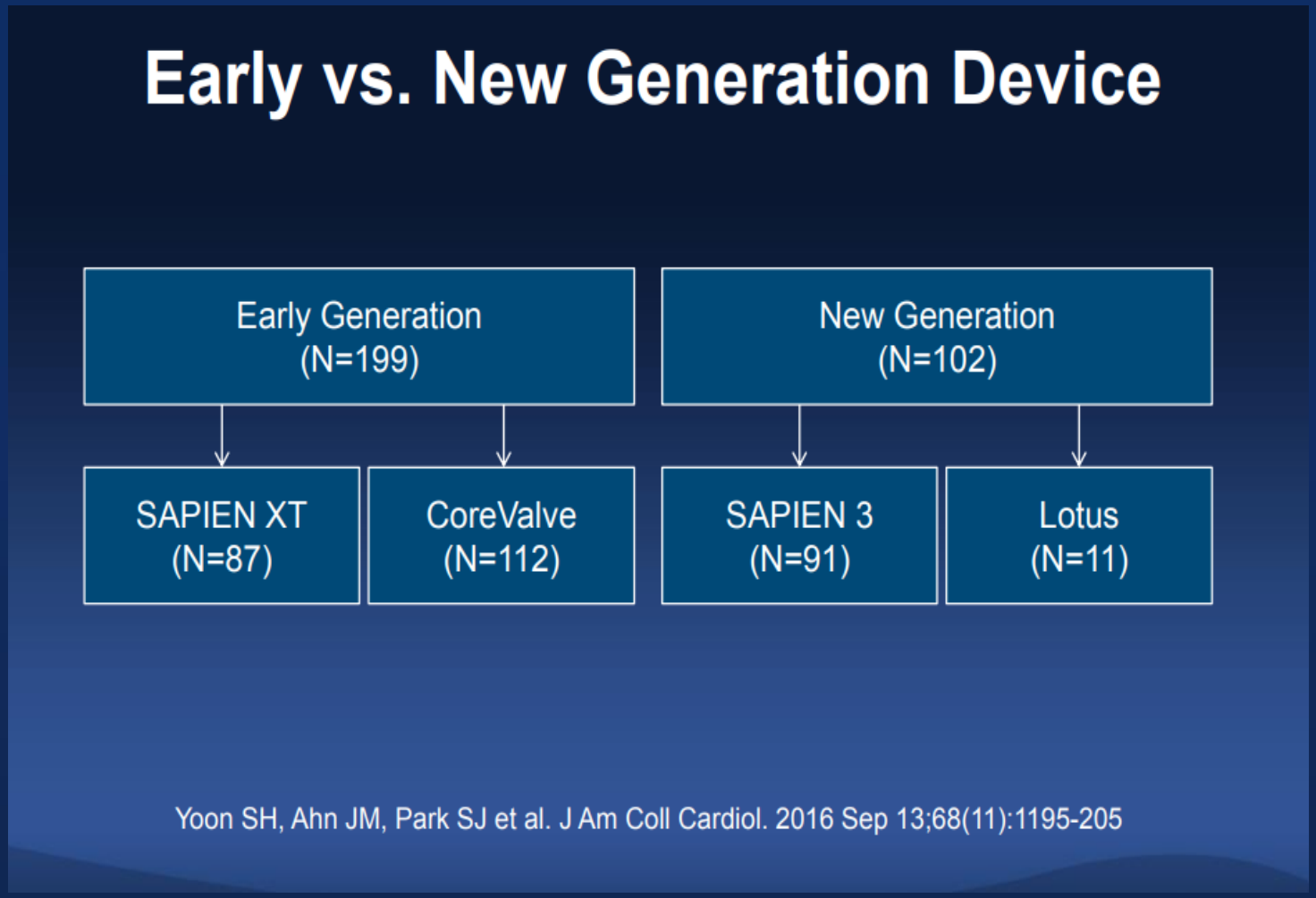



SH Yoon et al. JACC 2017;69:2579-89

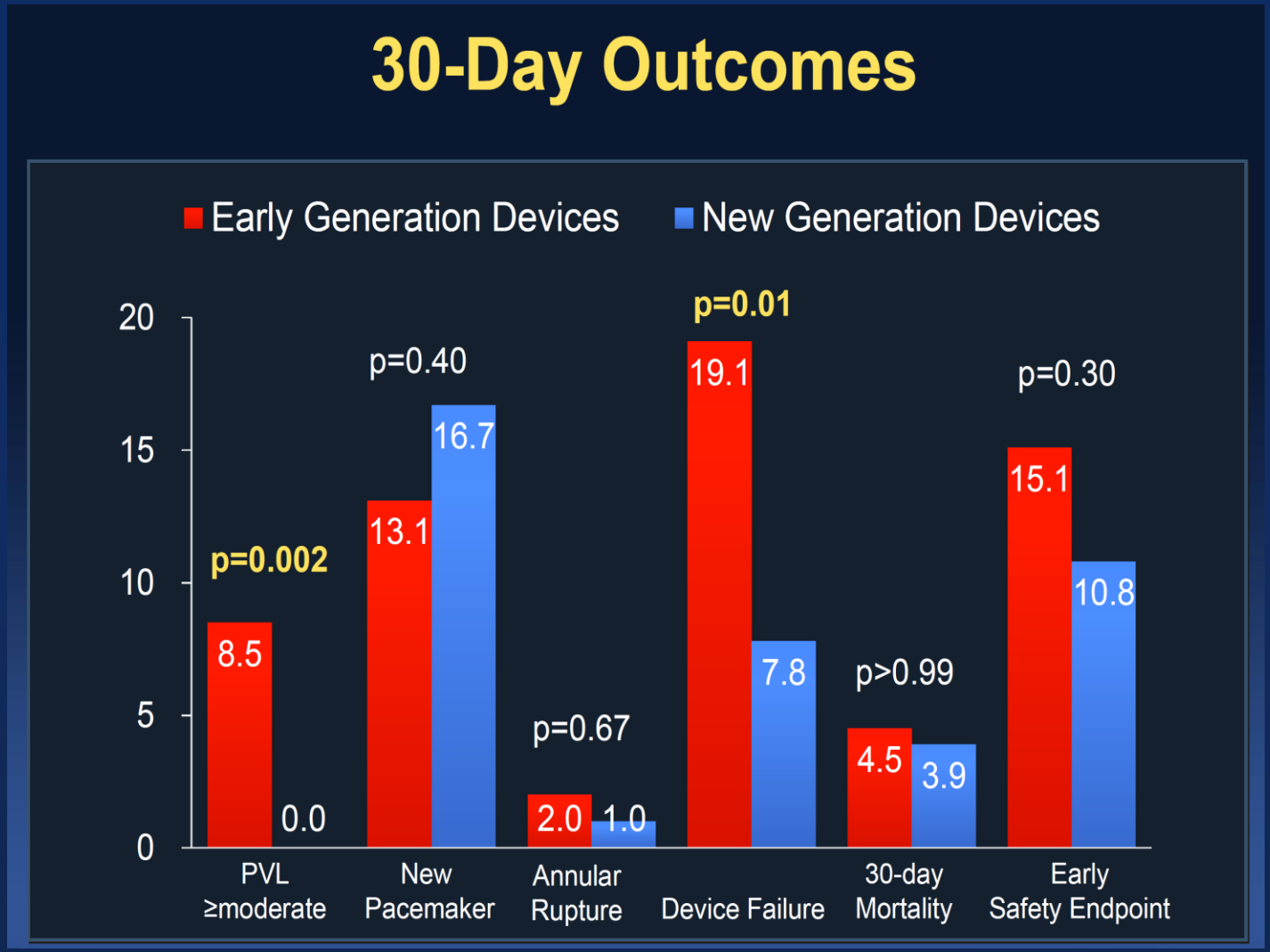
# 2-year outcomes of Bicuspid vs. Tricuspid with PS matching



# Bicuspid TAVR in Asians

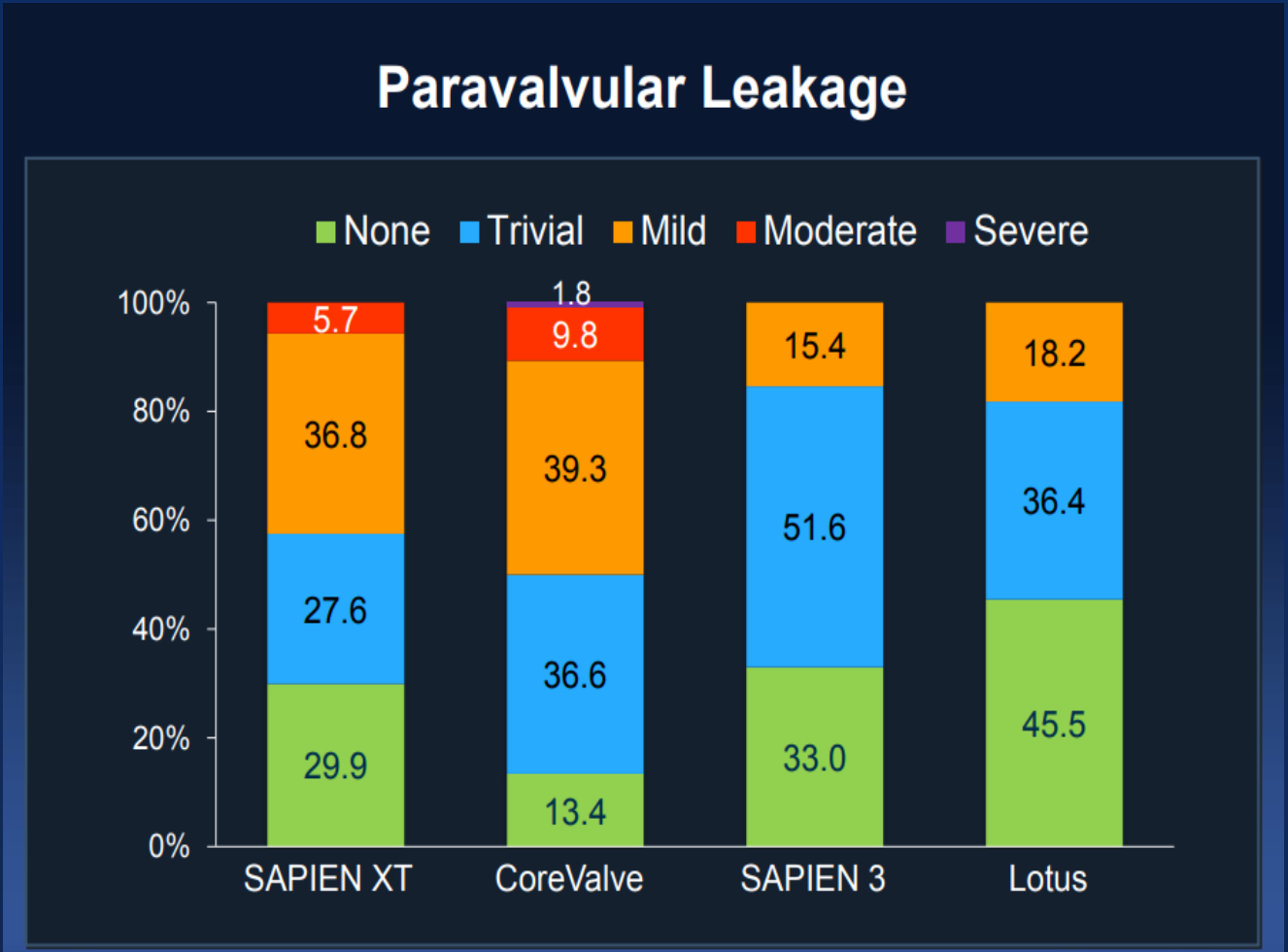


# Bicuspid TAVR in Asians



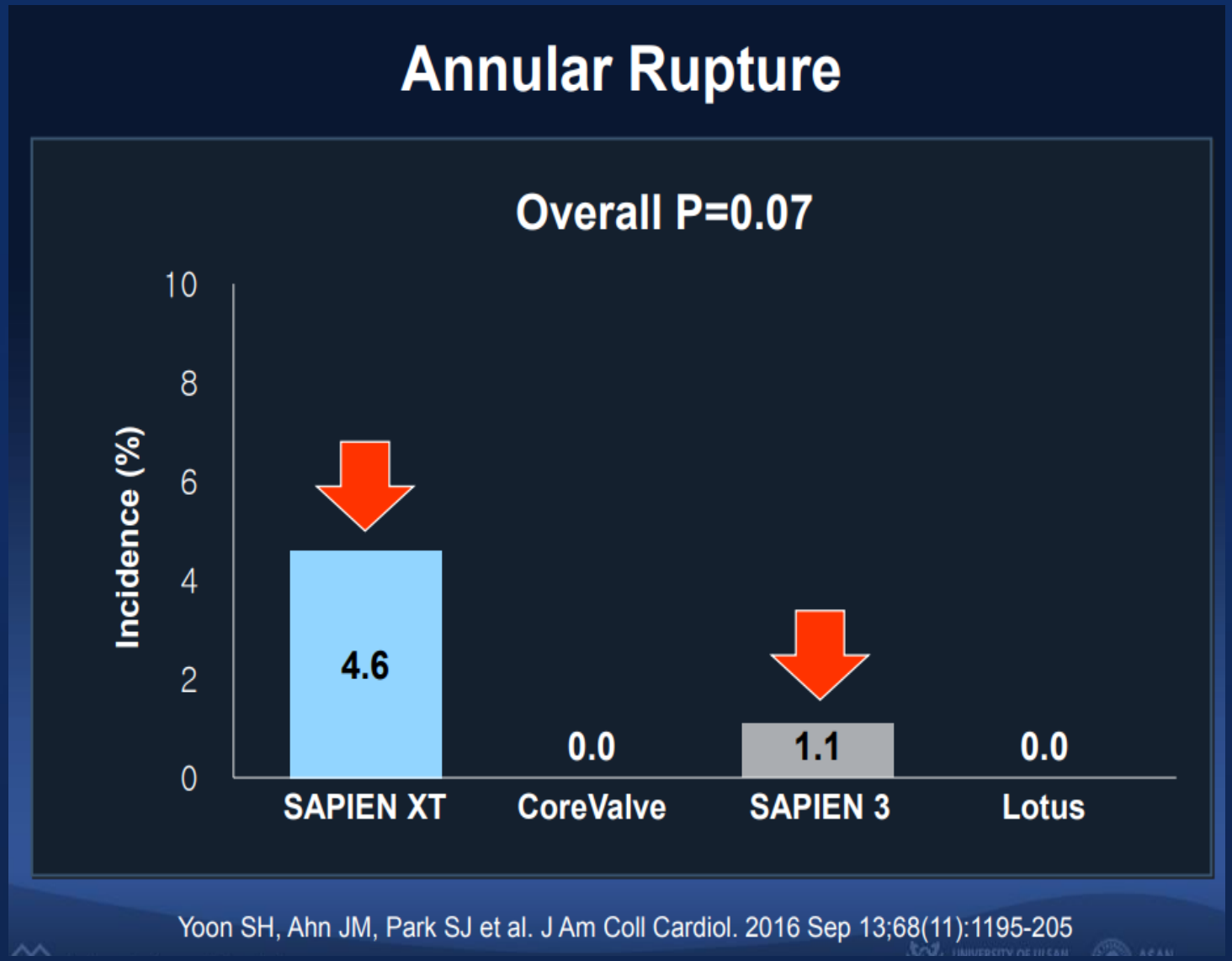

*Yoon SH, Ahn JM, Park SJ et al. JACC 2016;68(11):1195-20*

# Bicuspid TAVR in Asians



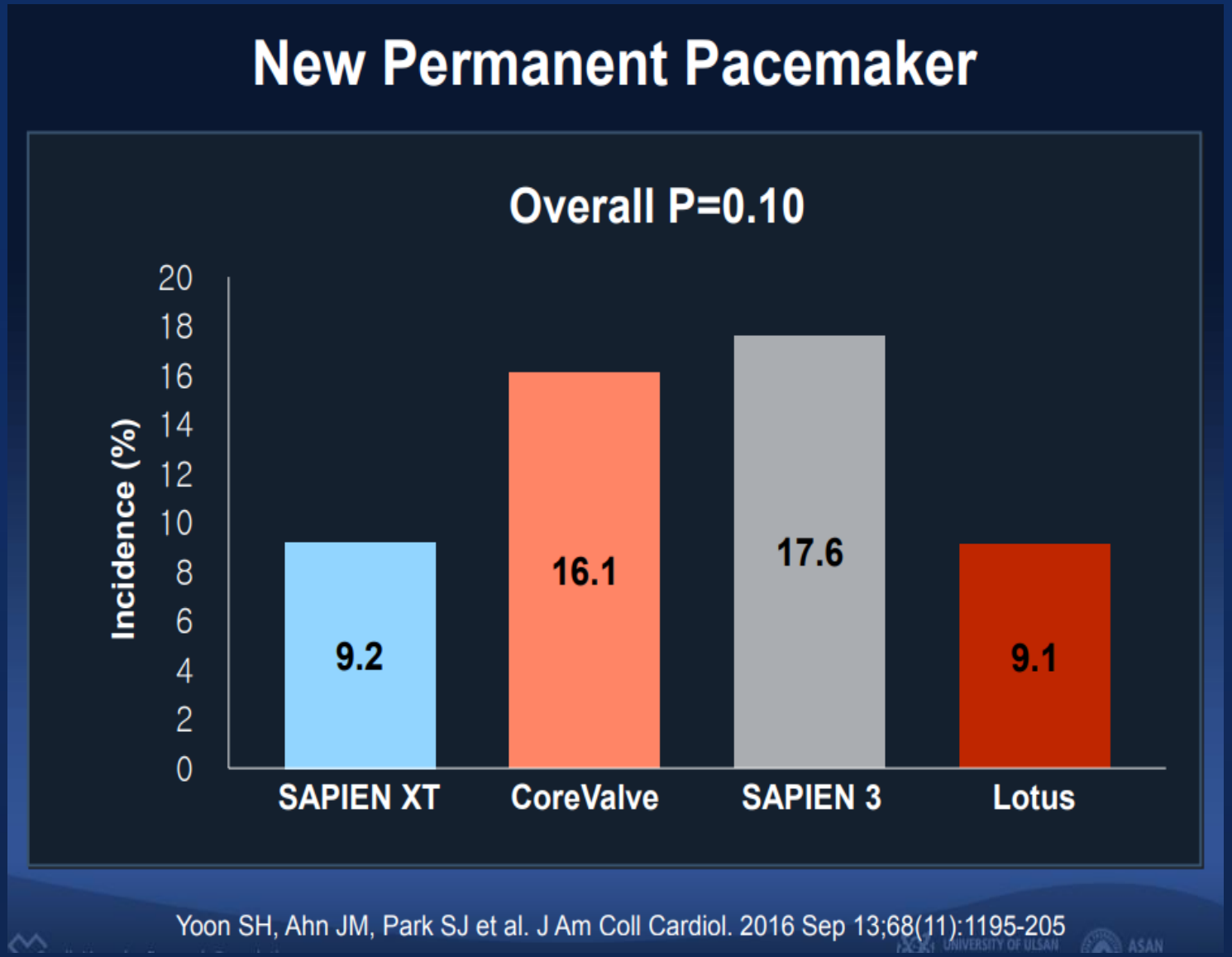

Yoon SH, Ahn JM, Park SJ et al. J Am Coll Cardiol. 2016 Sep 13;68(11):1195-205

# Bicuspid TAVR in Asians




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

# 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:

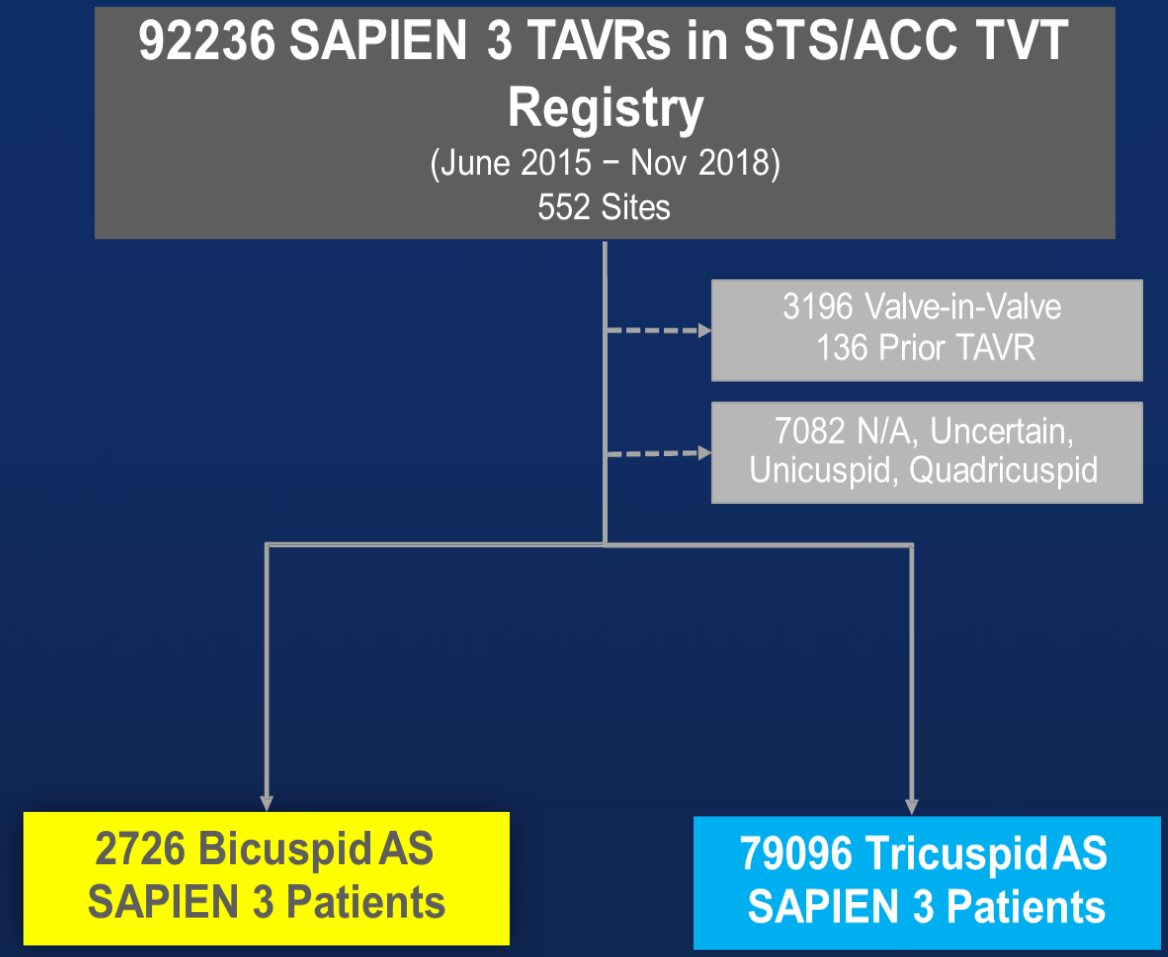
## An analysis of the STS/ACC TVT Registry

# 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

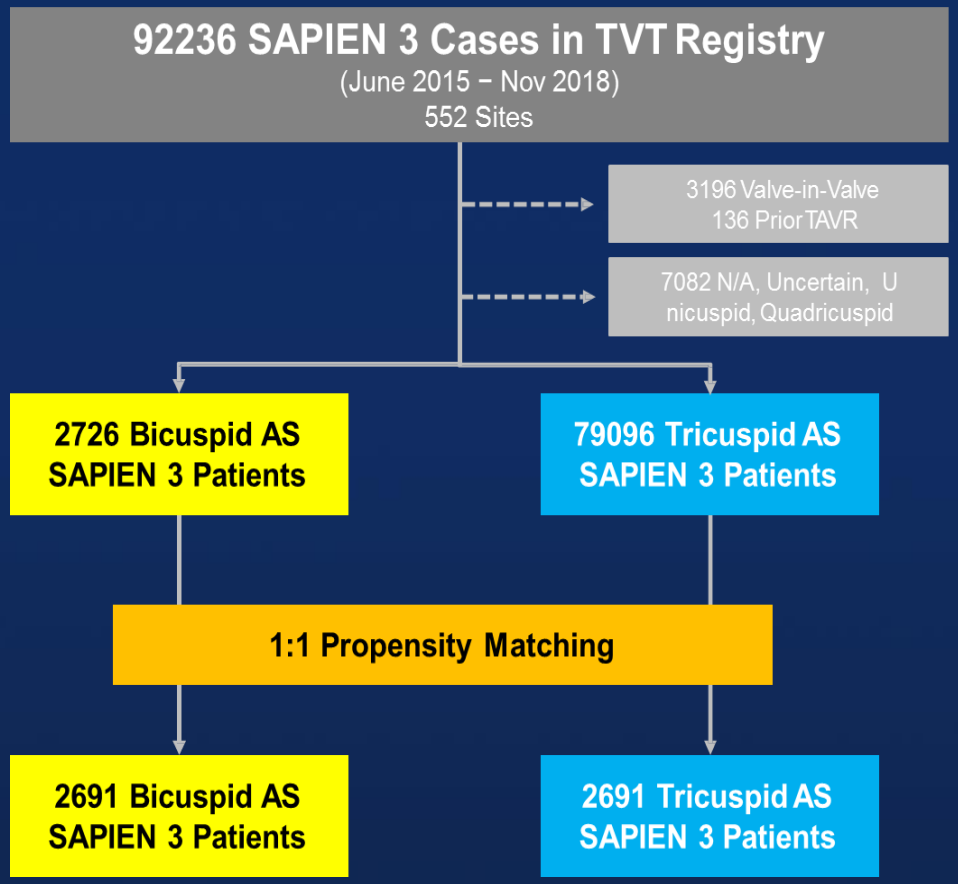


# STS/ACC TVT Registry

## Baseline Characteristics – Unadjusted

| Characteristic<br>% or mean ± SD | Bicuspid AS<br>(n=2726) | Tricuspid AS<br>(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<br>% or mean ± SD | Bicuspid AS<br>(n=2691) | Tricuspid AS<br>(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<br>% or mean ± SD | Bicuspid AS<br>(n=2691) | Tricuspid AS<br>(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

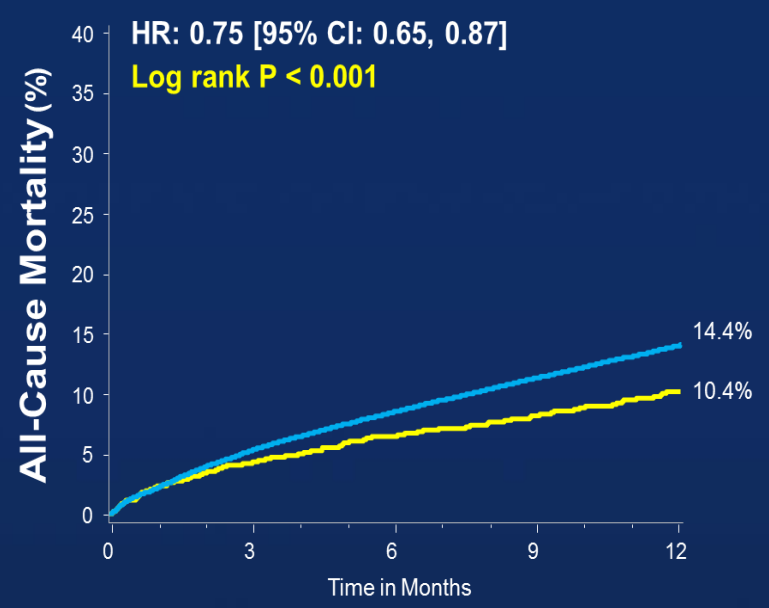
| Characteristic<br>% or mean ± SD | Bicuspid AS<br>(n=2691) | Tricuspid AS<br>(n=2691) | p-value |
|---|---|---|---|
| Device success | 96.5 | 96.6 | 0.87 |
| Procedure Time, min | 100.7 ± 51.80 | 98.2 ± 52.09 | 0.08 |
| Fluoroscopy Time, min | 18.5 ± 10.96 | 17.1 ± 10.17 | <0.0001 |
| **Conversion 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 |

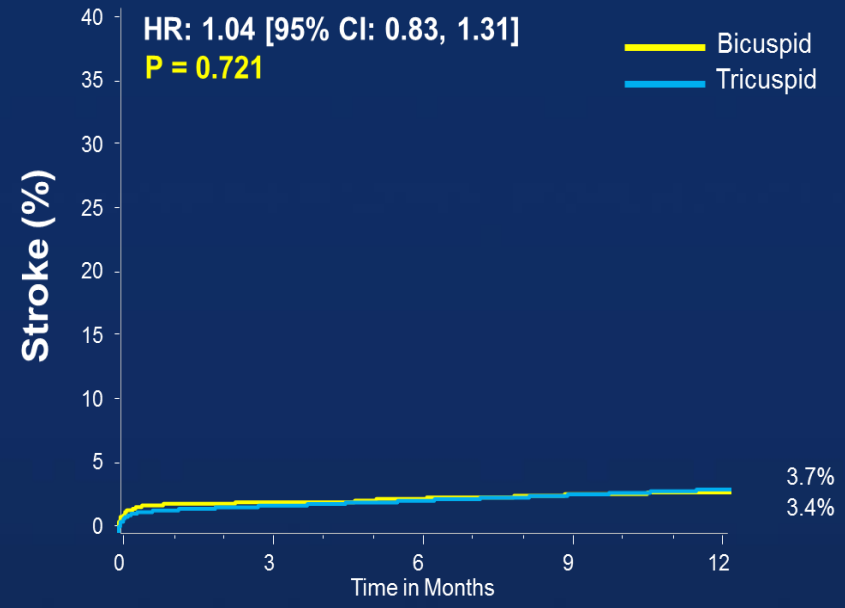
# 1-Year Mortality and All Stroke

## Unadjusted Cohort




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

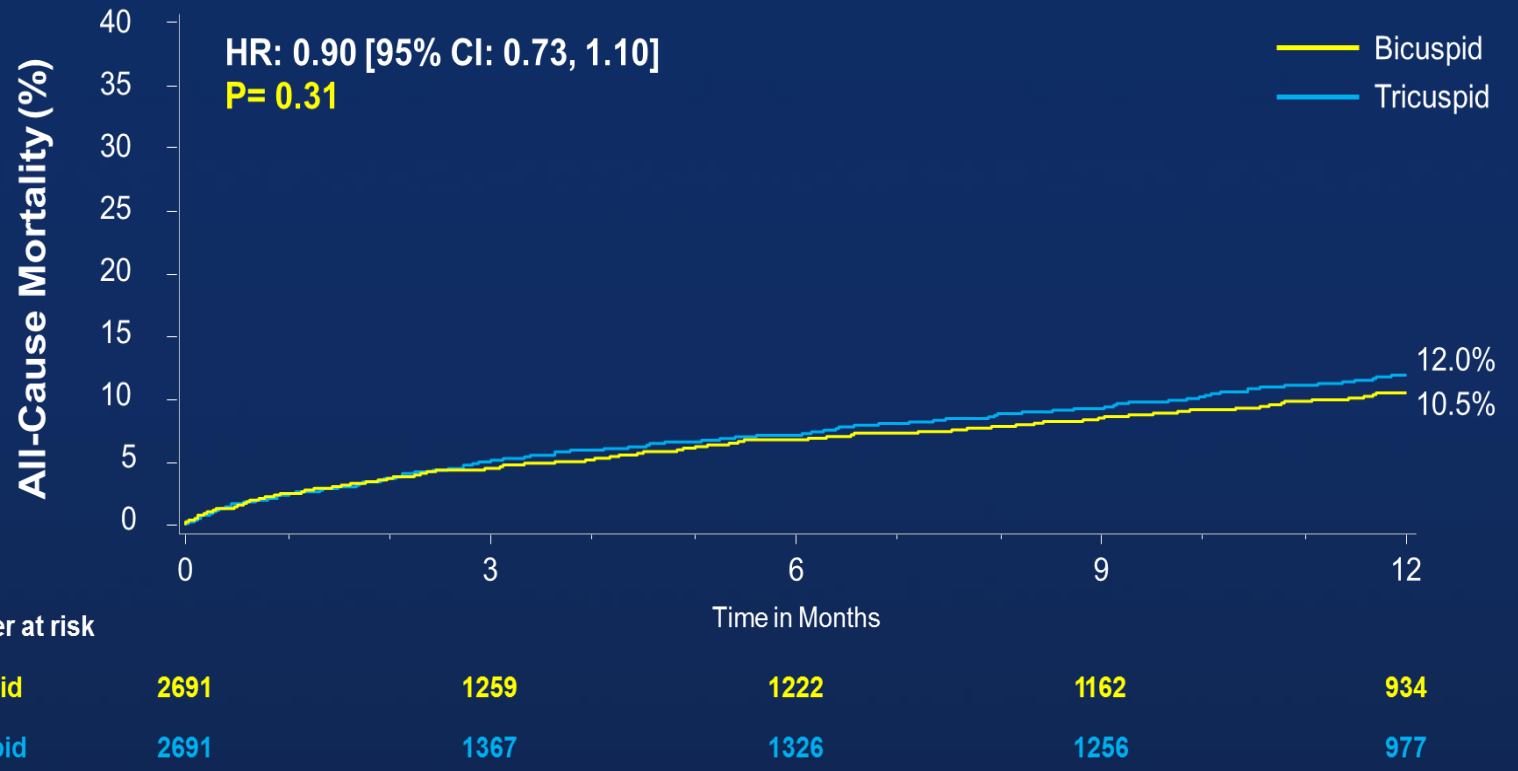
Number at risk




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

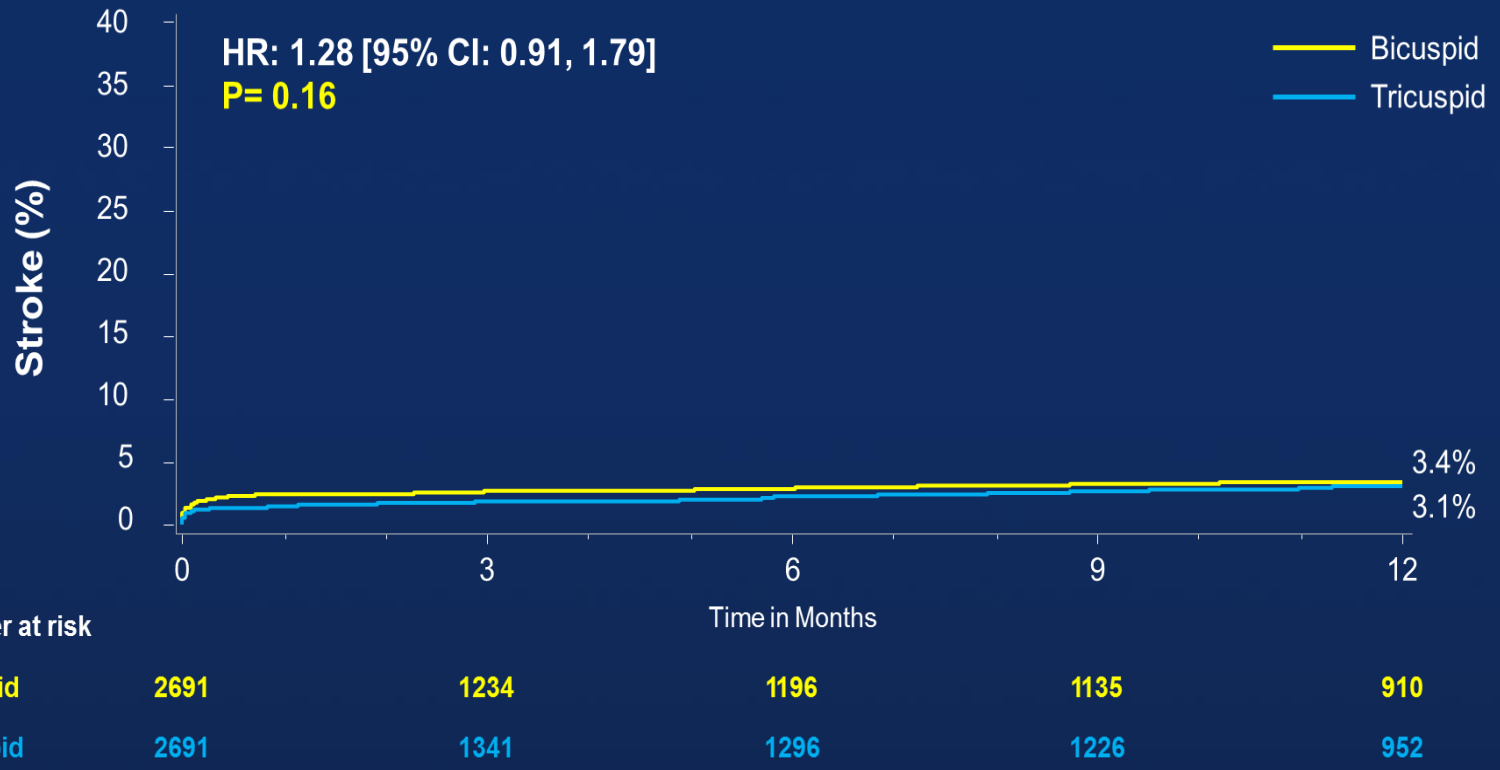
Number at risk

# 1-Year Mortality:
## Matched



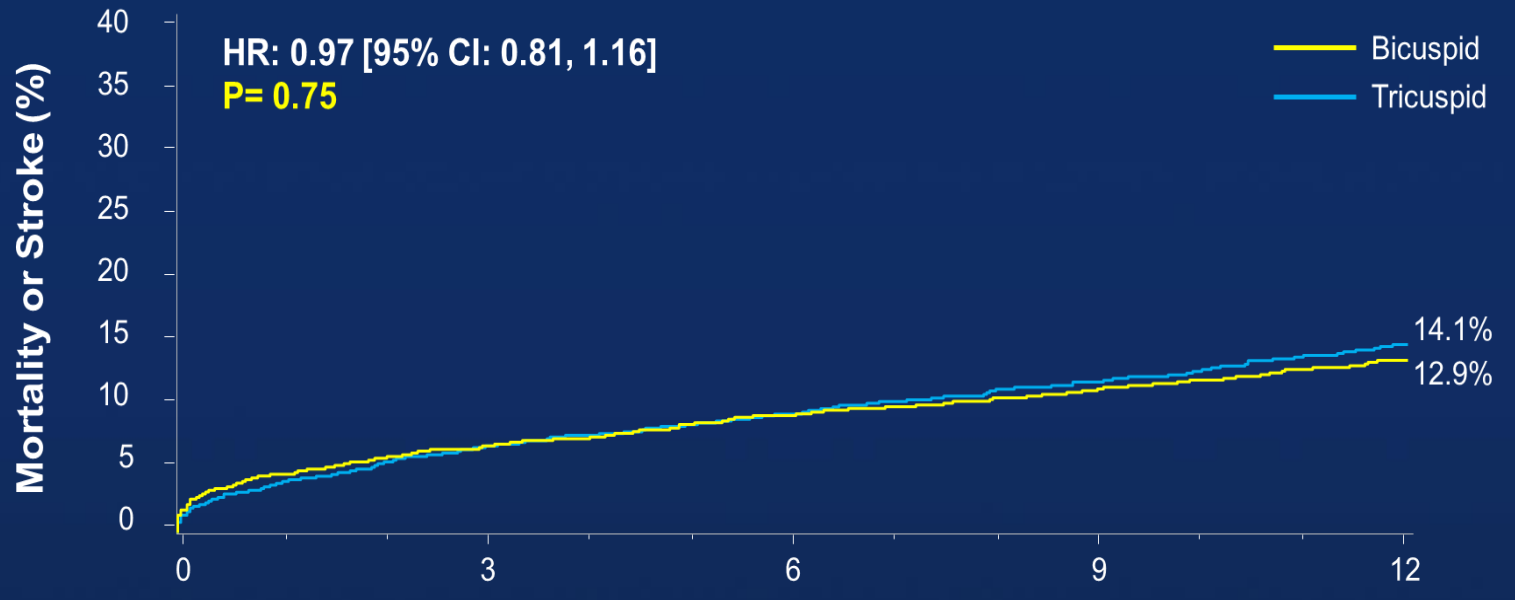

| Number at risk | | | | | |
|---|---|---|---|---|---|
| Bicuspid | 2691 | 1259 | 1222 | 1162 | 934 |
| Tricuspid | 2691 | 1367 | 1326 | 1256 | 977 |

# 1-Year Stroke:
## Matched



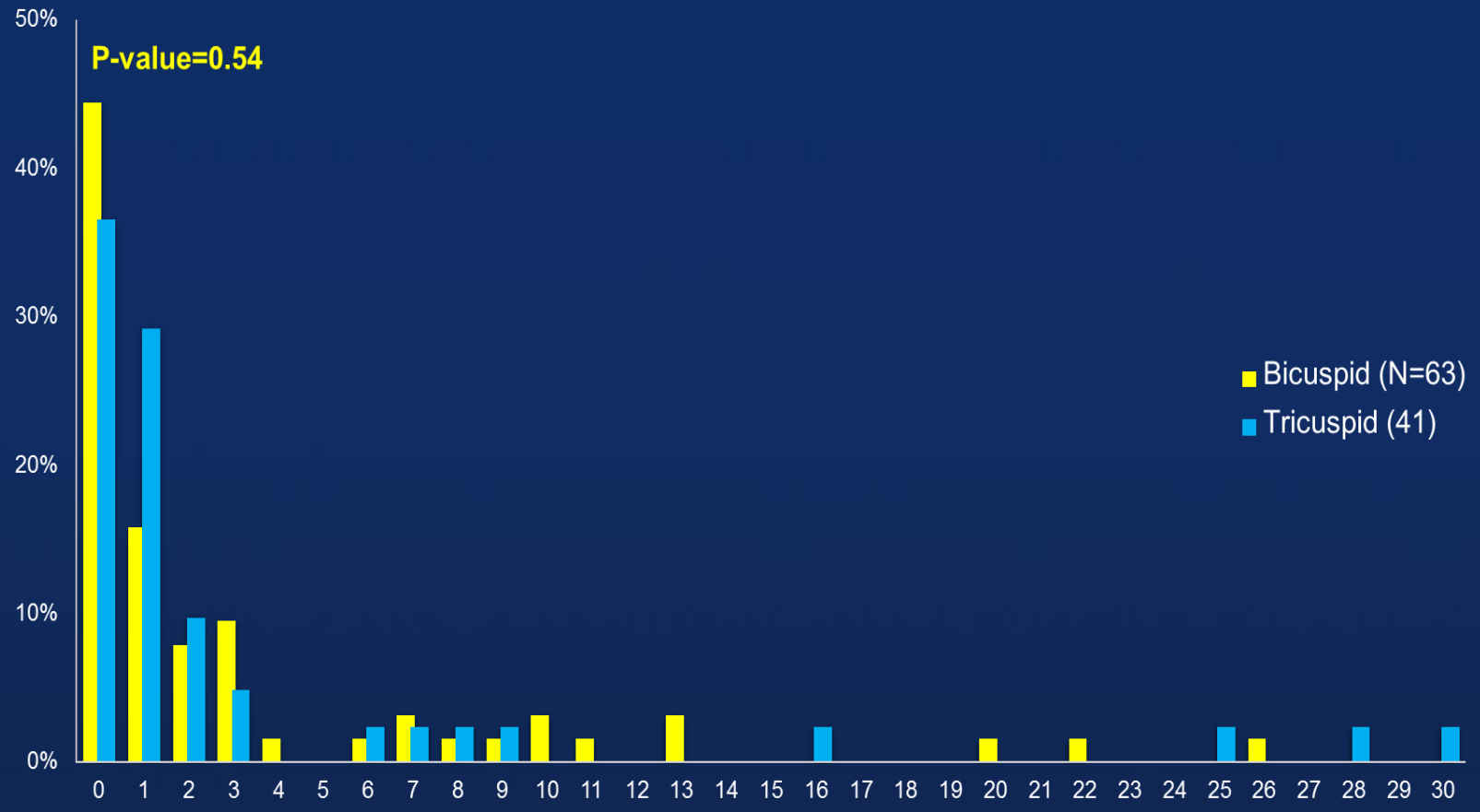

| Number at risk | | | | | |
|---|---|---|---|---|---|
| Bicuspid | 2691 | 1234 | 1196 | 1135 | 910 |
| Tricuspid | 2691 | 1341 | 1296 | 1226 | 952 |

# 1-Year Mortality or Stroke:
## Matched

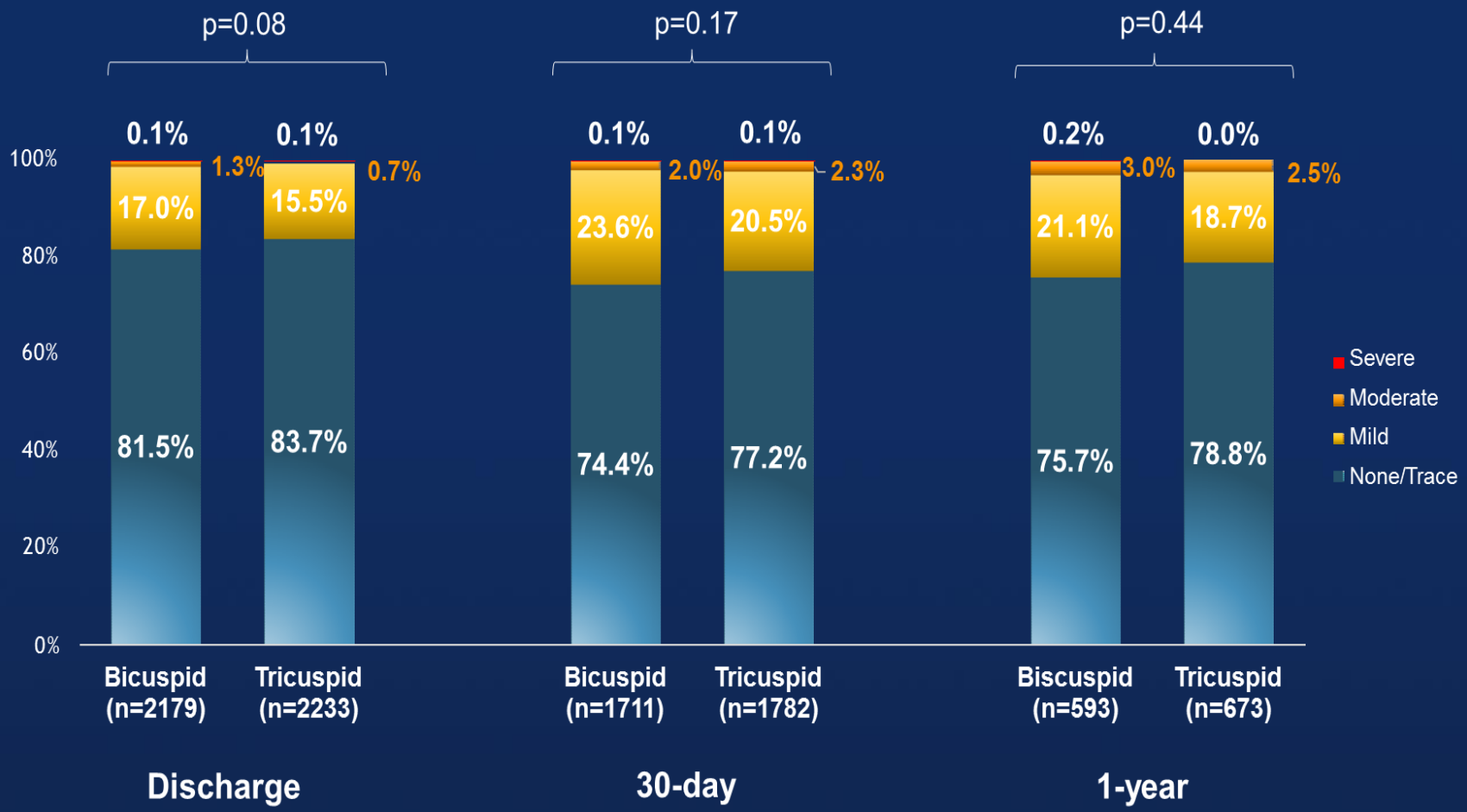



| Number at risk | | | | | |
|---|---|---|---|---|---|
| Bicuspid | 2691 | 1234 | 1196 | 1135 | 910 |
| Tricuspid | 2691 | 1341 | 1296 | 1226 | 952 |

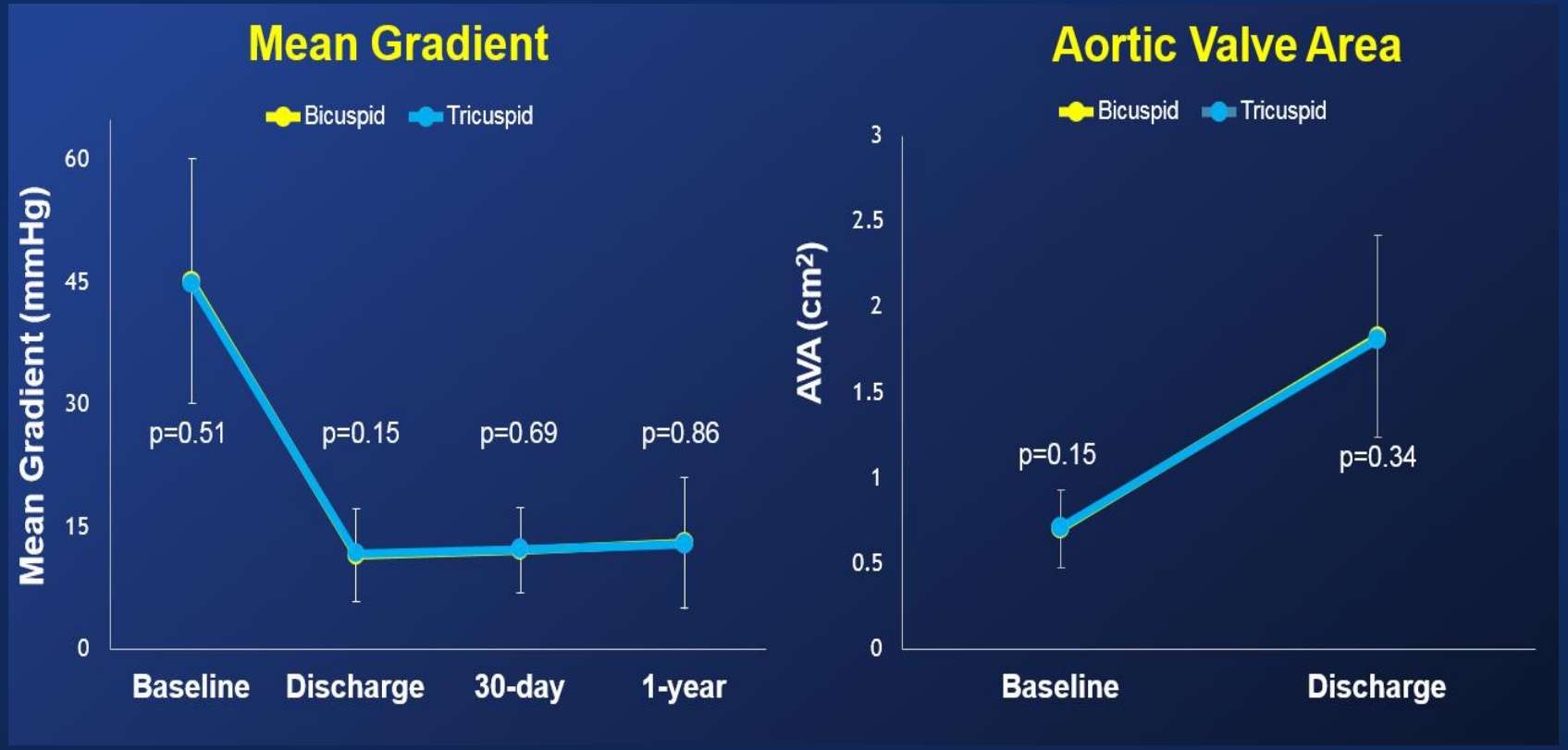
# Timing of All-Stroke Events



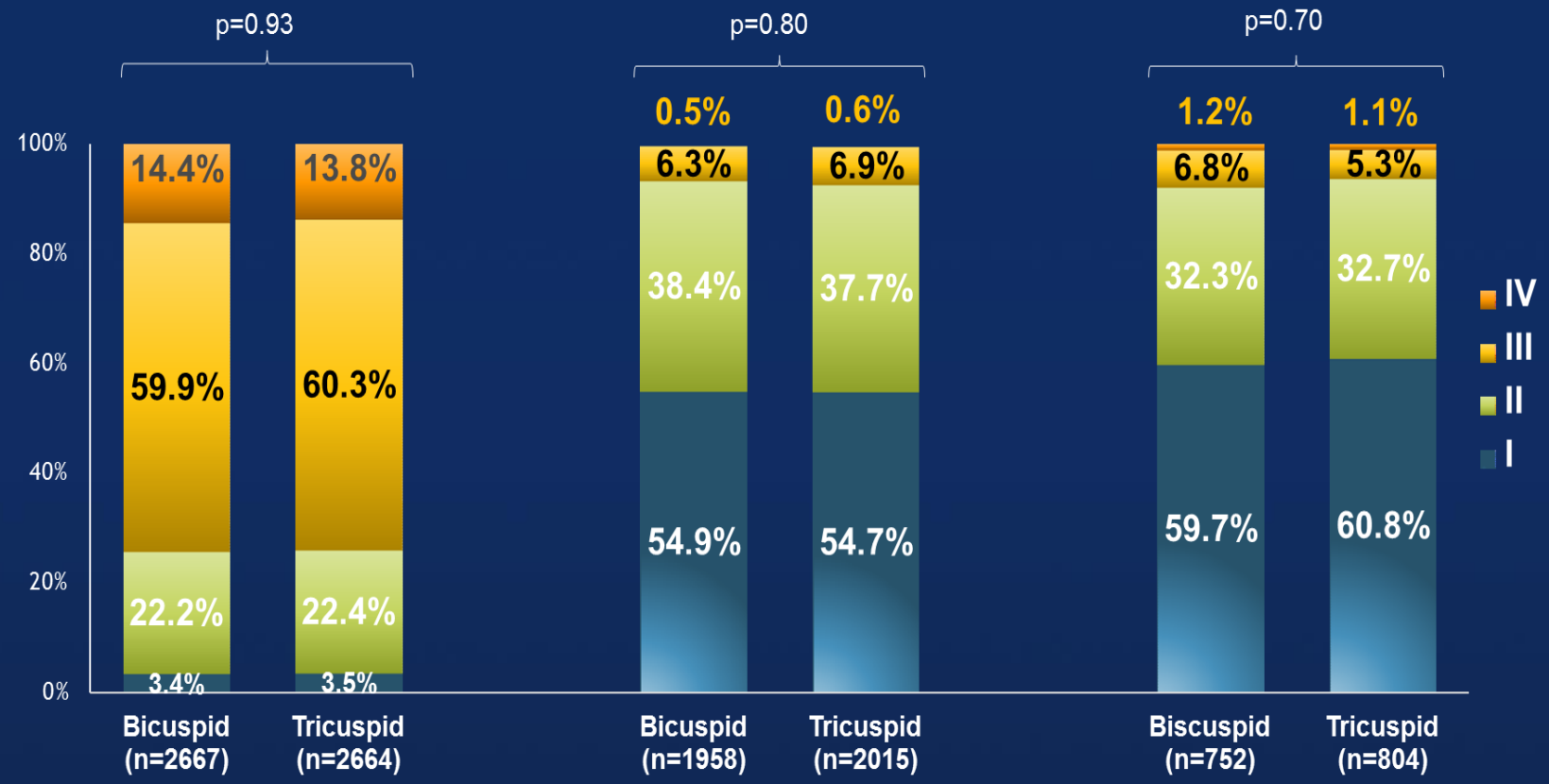
# Paravalvular Leak – Matched



# Hemodynamics – Matched



# NYHA Class – Matched



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

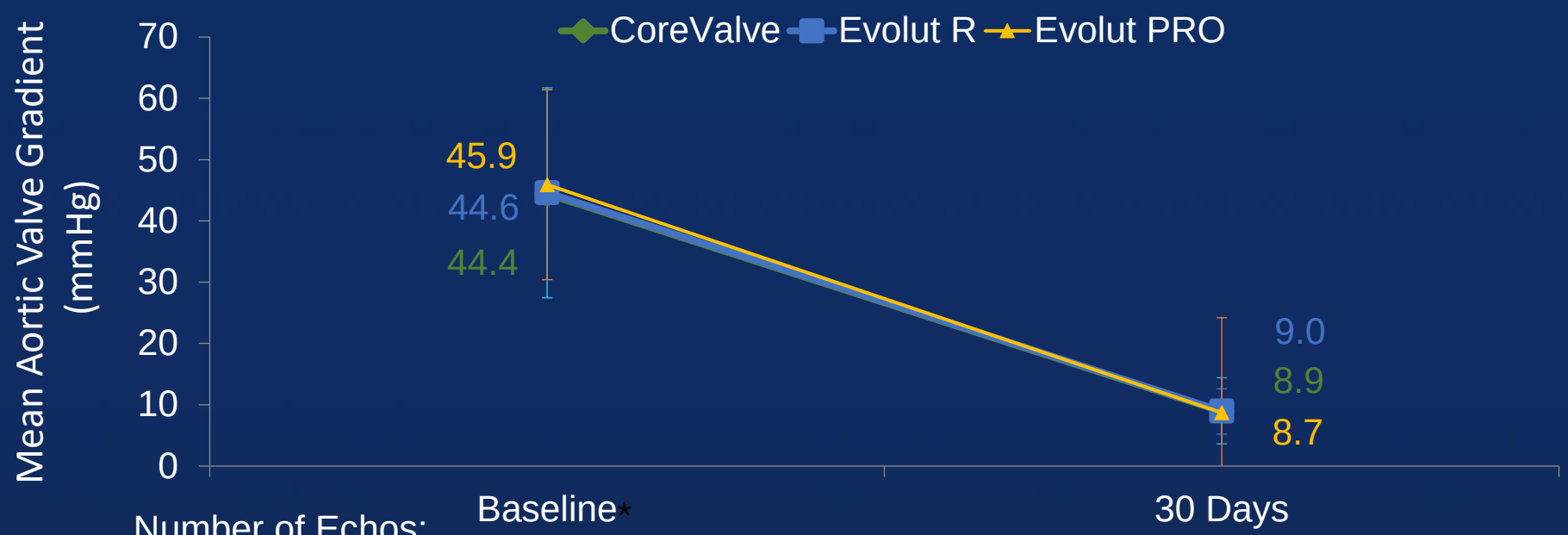
| Outcome, % | CoreValve (N=319) | Evolut R (N=677) | Evolut PRO (N=236) | *P*-Value | |
|---|---|---|---|---|---|
| | | | | CoreValve vs. Evolut R | Evolut R vs. PRO |
| All-cause mortality | 5.4 | 2.4 | 3.0 | 0.01 | 0.57 |
| Stroke | 1.9 | 3.3 | 5.6 | 0.23 | 0.12 |
| Myocardial infarction | 0.3 | 0.2 | 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

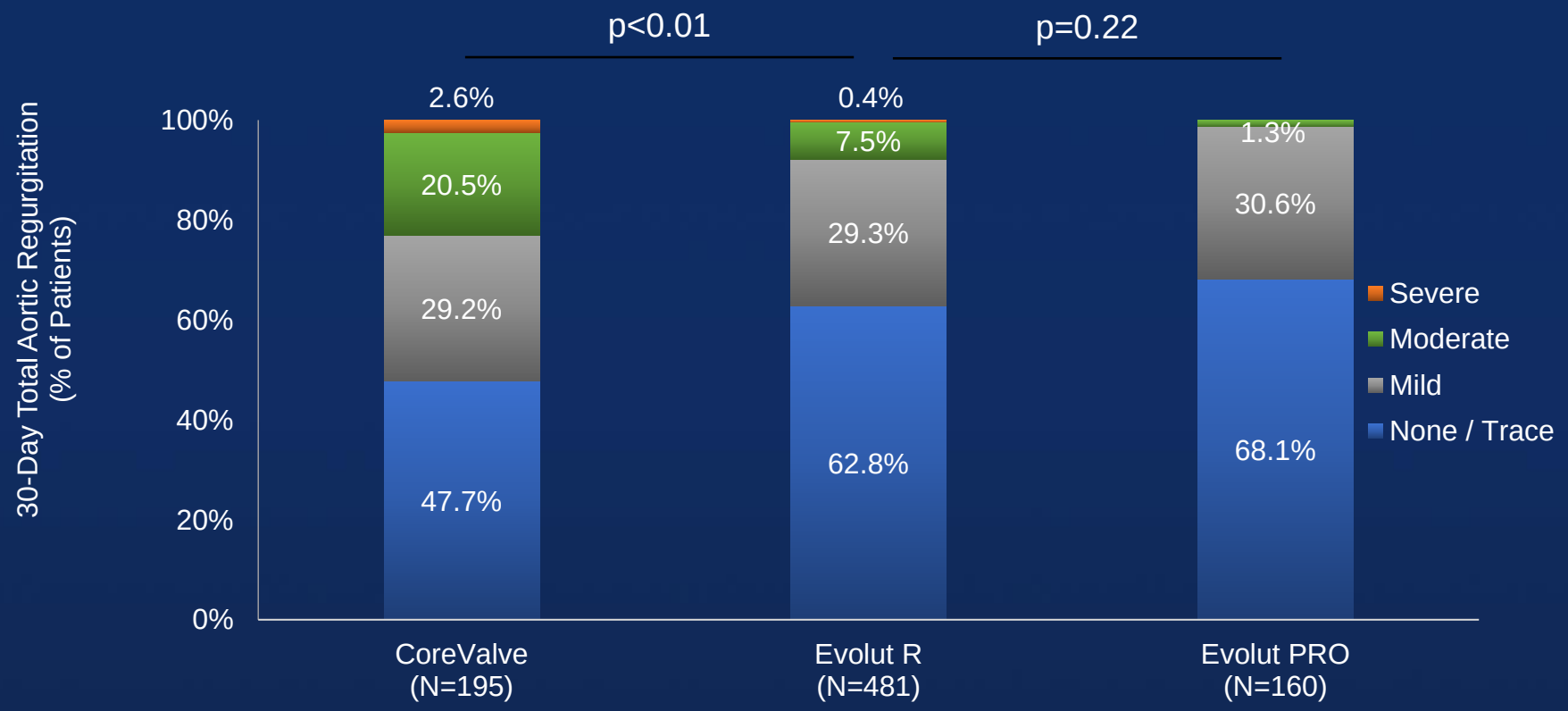



| Number of Echos: | Baseline* | 30 Days |
|---|---|---|
| CoreValve | 314 | 190 |
| Evolut R | 663 | 478 |
| Evolut PRO | 236 | 156 |

*Baseline subjects are all subjects attempted for the procedure

**John K. Forrest, TVT2019**

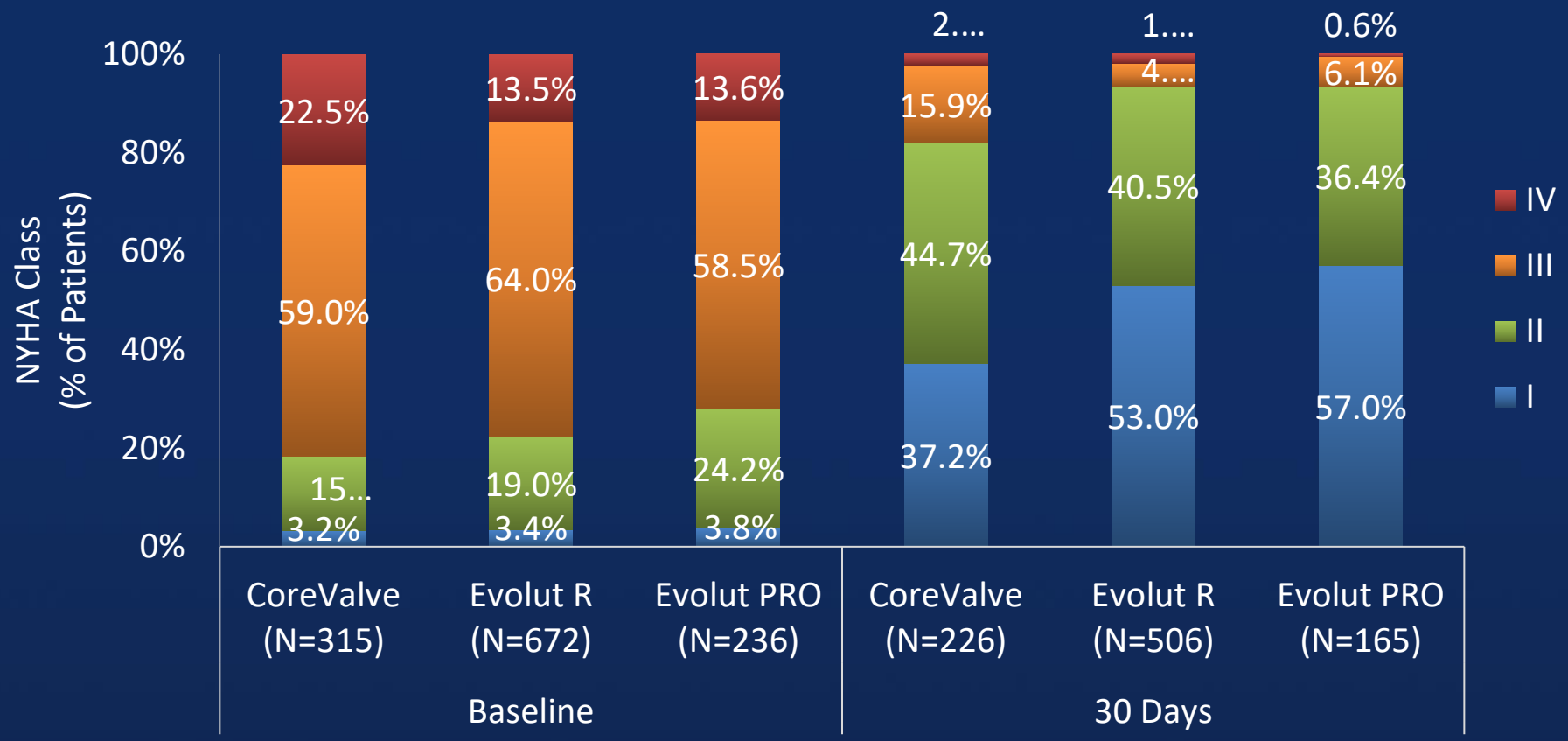
# 30d AR: Self-expanding valve in BAV from STS/ACC TVT registry






John K. Forrest, TVT2019

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

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# 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 |



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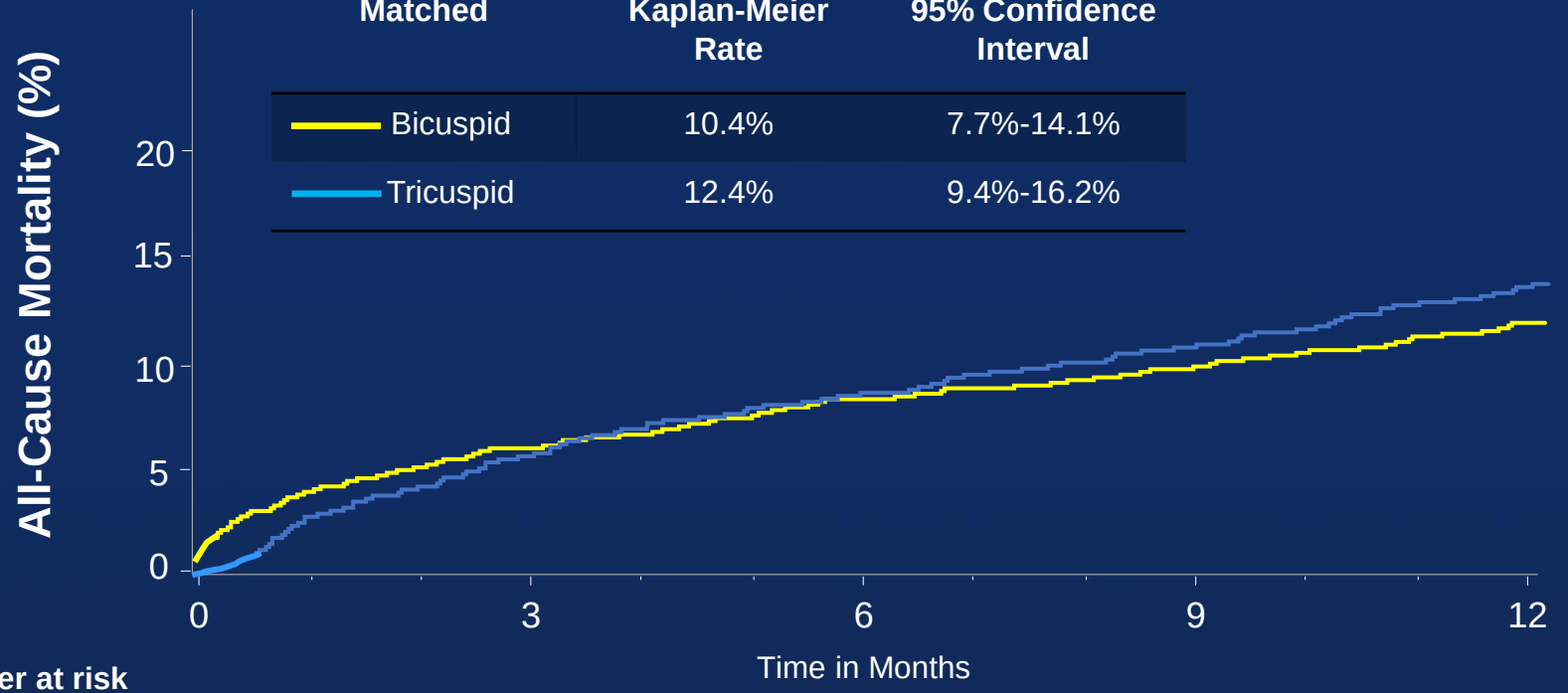
# 1-year mortality: TAVR in Bicuspid vs Tricuspid AS

## 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 |



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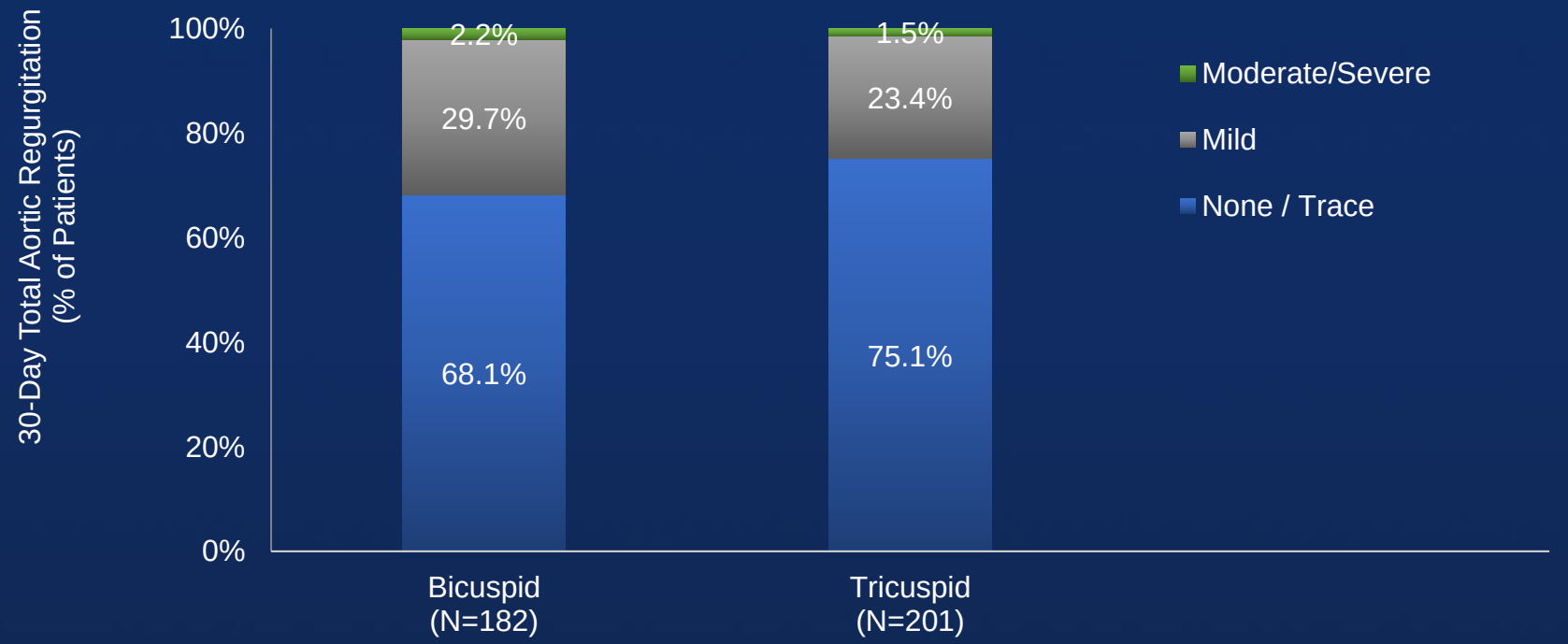
# 30d AR: TAVR in Bicuspid vs Tricuspid AS from STS/ACC TVT registry



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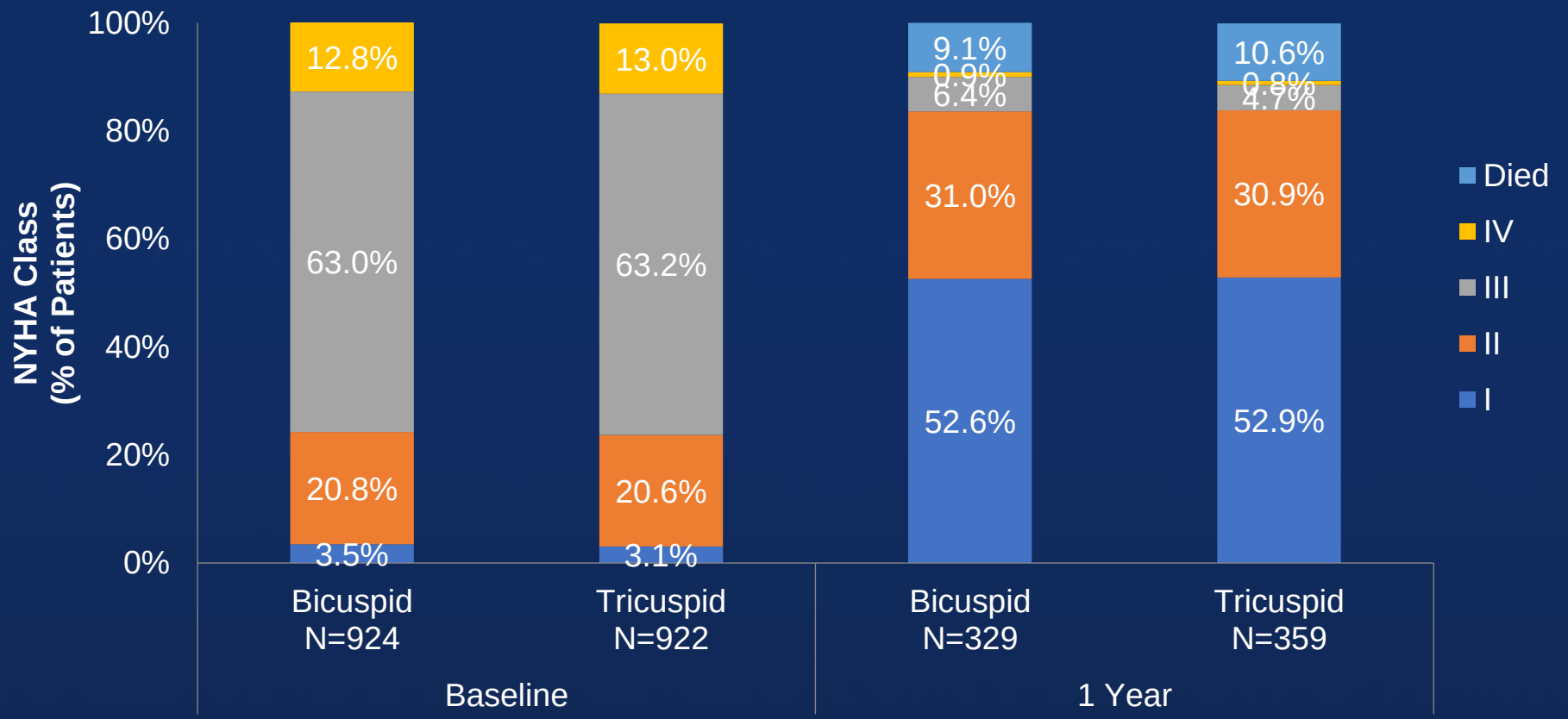
# NYHA class: TAVR in Bicuspid vs Tricuspid AS from STS/ACC TVT registry



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# 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 |



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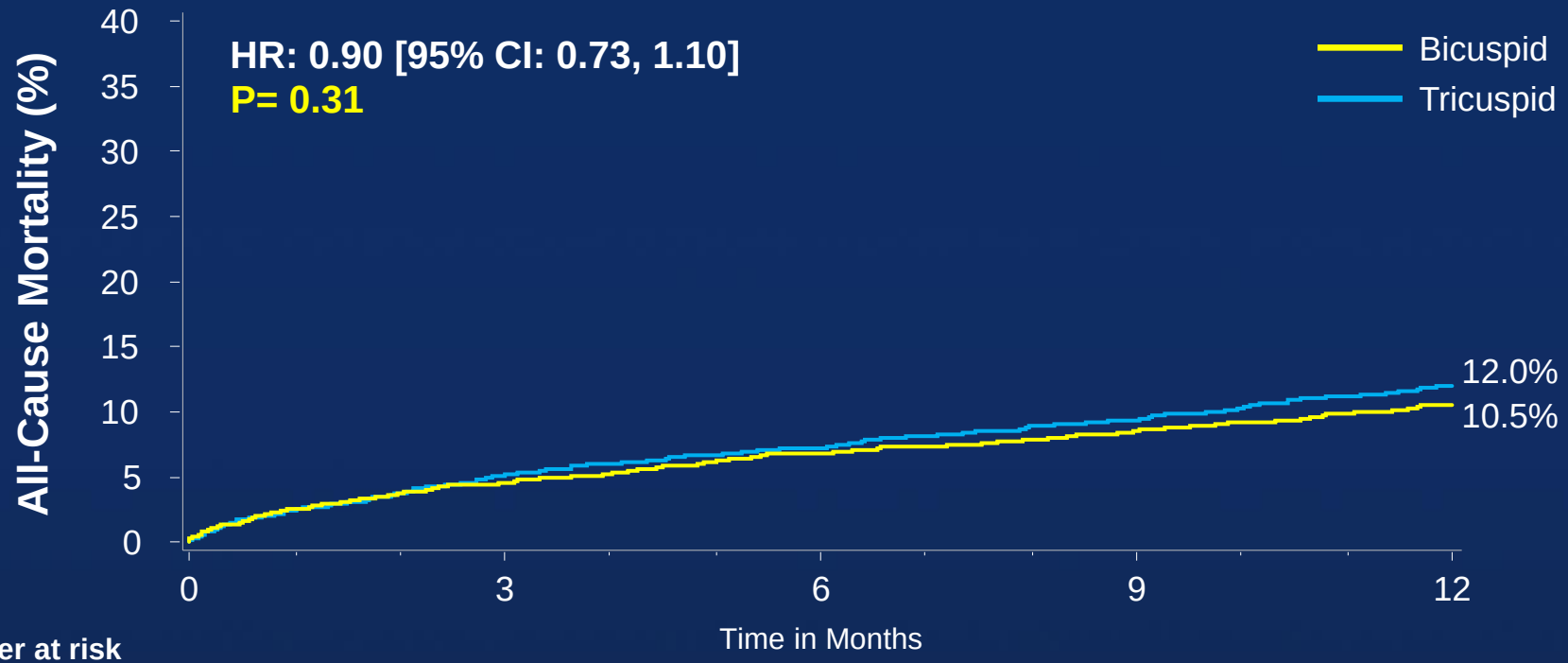
# 1-year mortality: TAVR in Bicuspid vs Tricuspid AS

from STS/ACC TVT Registry (PS matching)



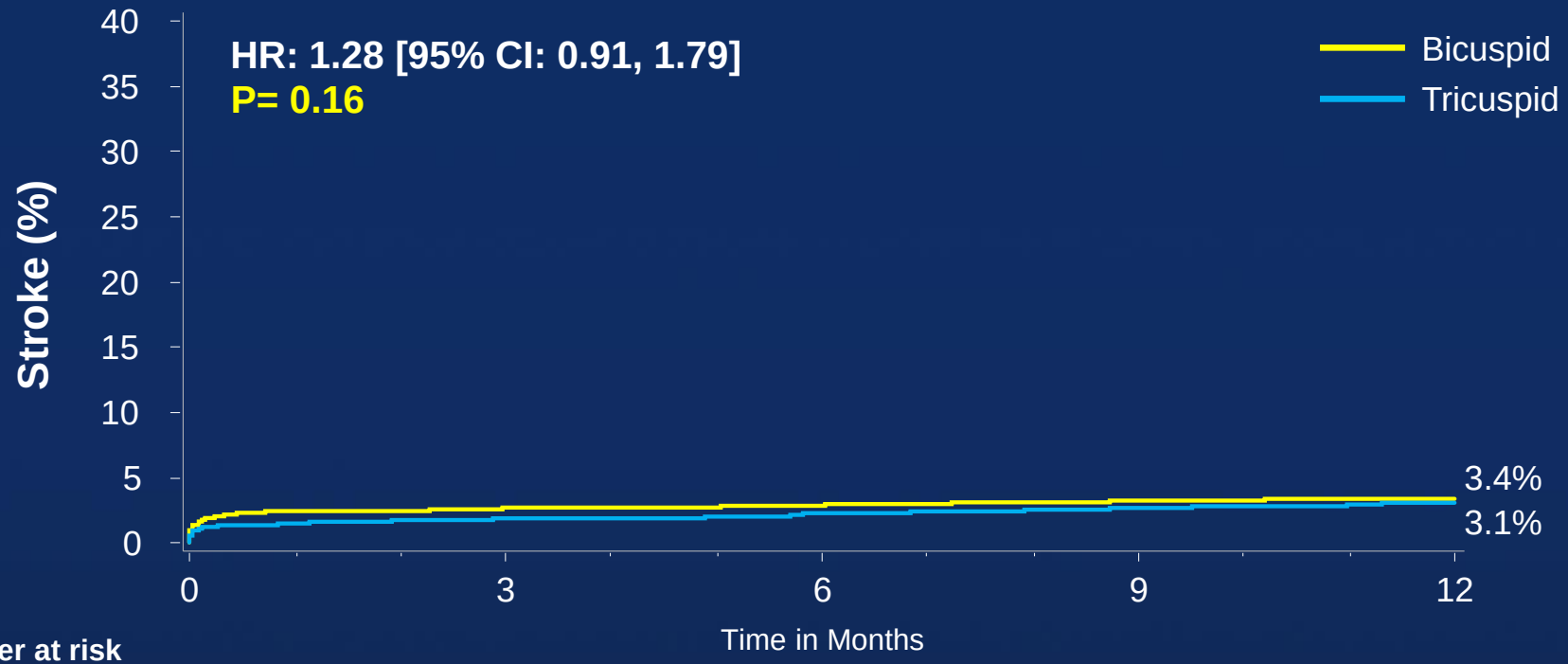

| Number at risk | | | | | |
|---|---|---|---|---|---|
| Bicuspid | 2691 | 1259 | 1222 | 1162 | 934 |
| Tricuspid | 2691 | 1367 | 1326 | 1256 | 977 |



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 |



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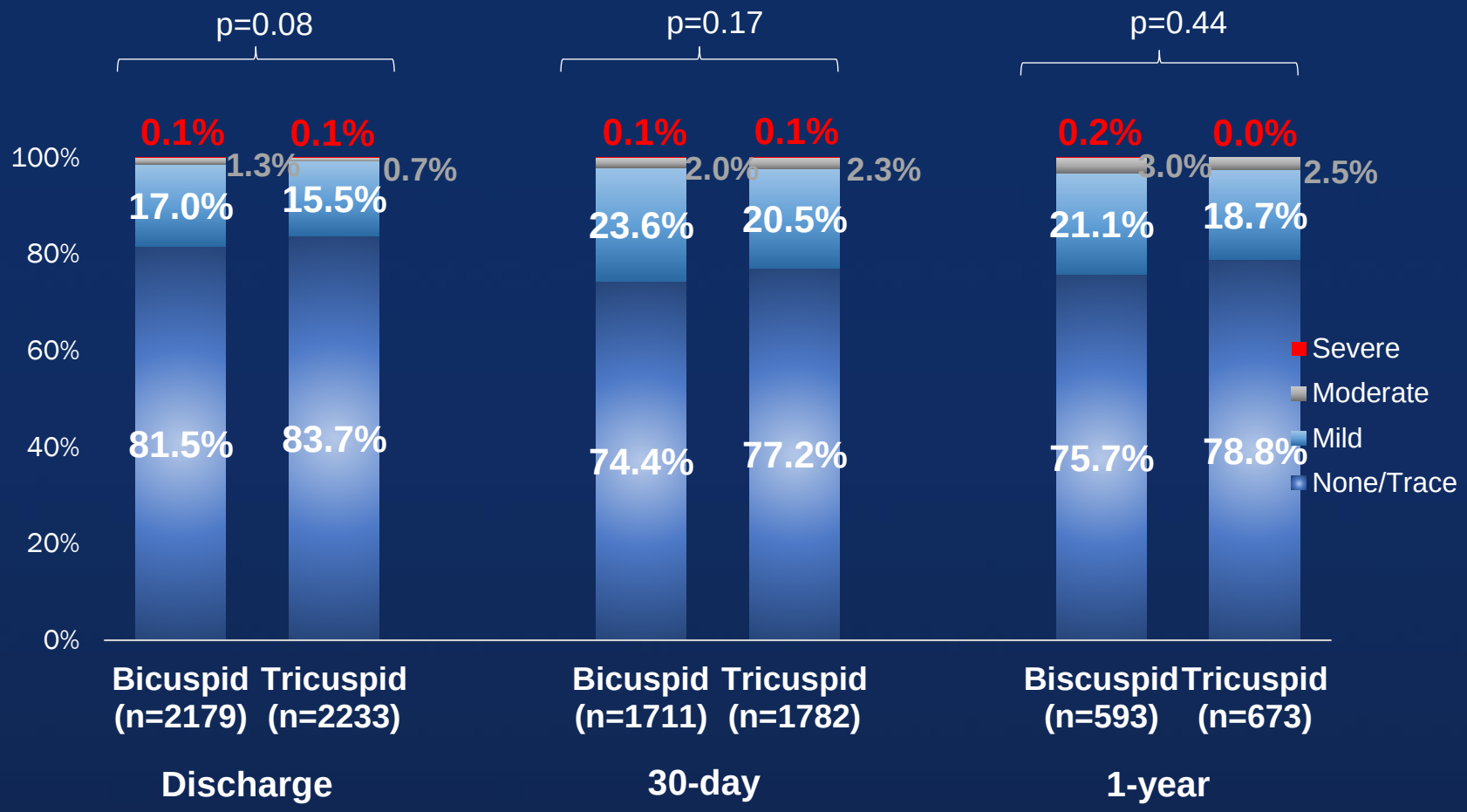
# Paravalvular leakage: TAVR in Bicuspid

## from STS/ACC TVT Registry (PS matching)

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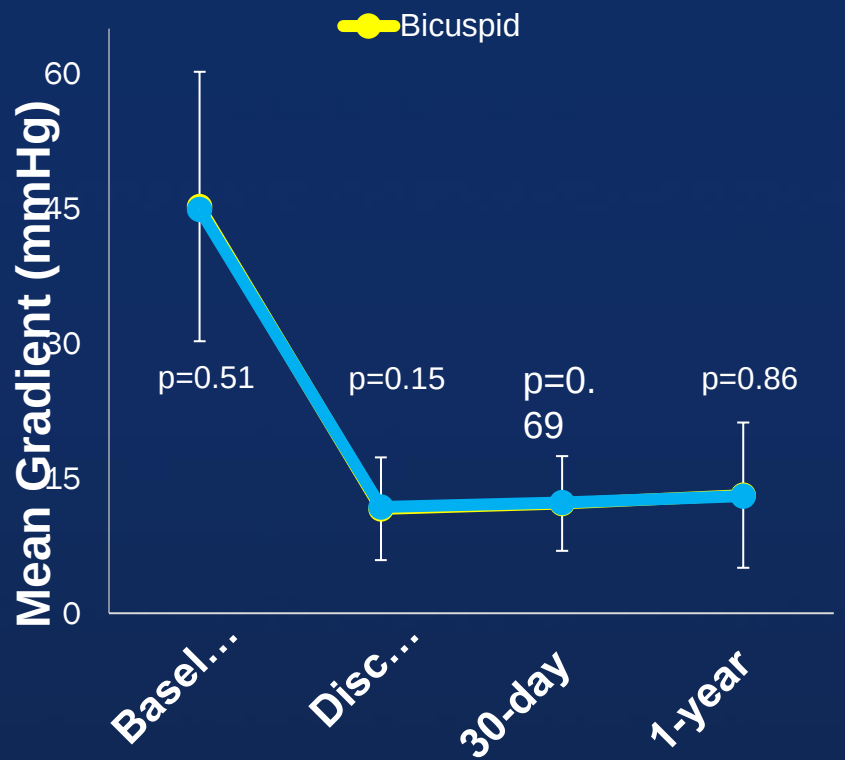
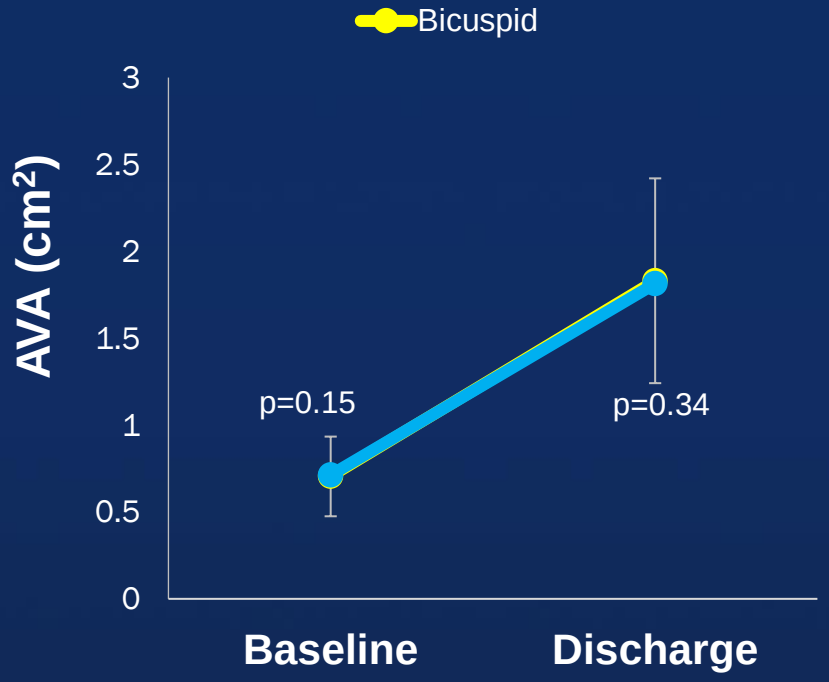
# Hemodynamics: TAVR in Bicuspid

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

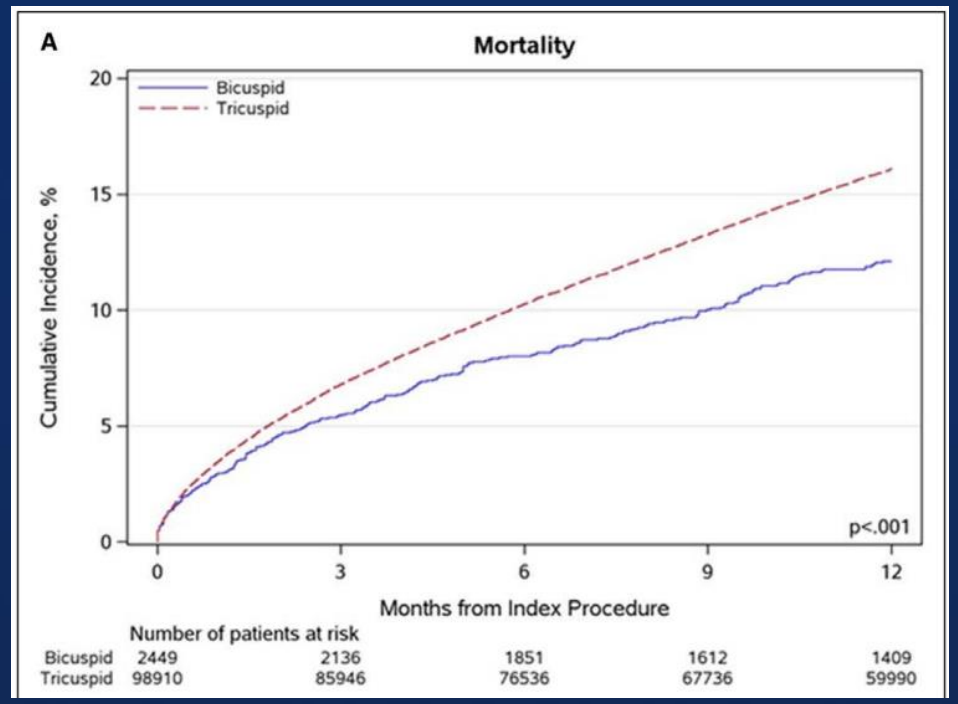
# In-hospital Outcomes of TAVR in Bicuspid vs Tricuspid AS from STS/ACC TVT Registry

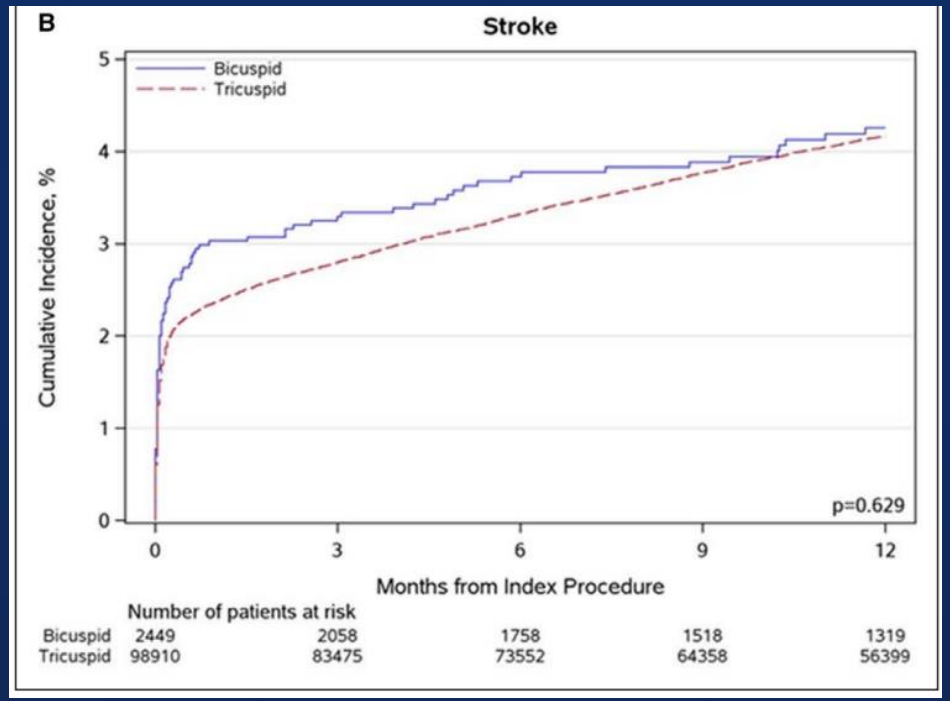
| Outcomes | Bicuspid N=5412 | Tricuspid N=165547 | P Value |
|---|---|---|---|
| In-hospital death, n (%) | 110 (2.0) | 3598 (2.2) | 0.484 |
| Observed/expected mortality ratio (95% CI) | 0.40 (0.33-0.48) | 0.31 (0.30-0.32) | 0.006 |
| In-hospital stroke, n (%) | 117 (2.2) | 3131 (1.9) | 0.151 |
| In-hospital 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

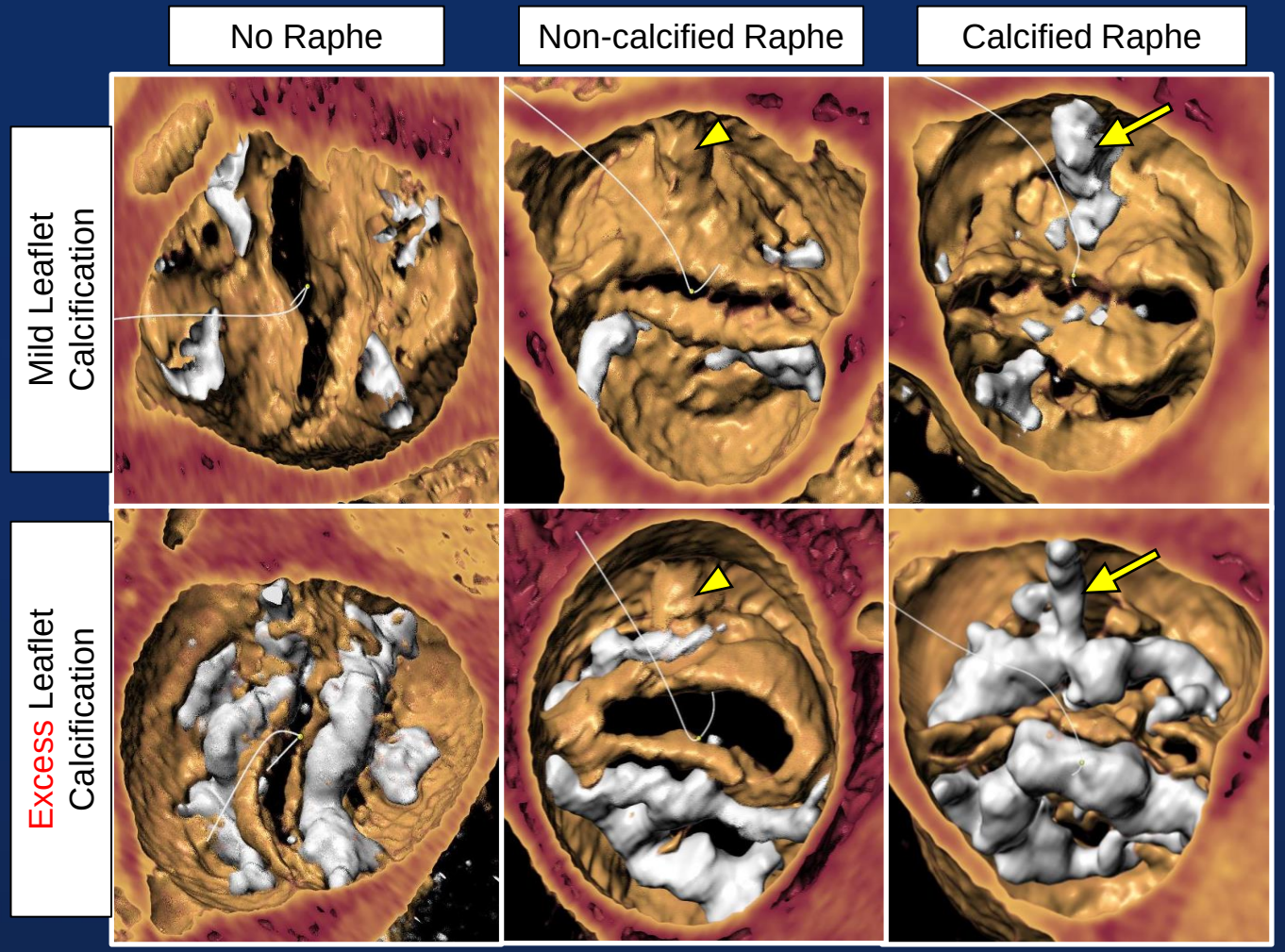
| Characteristic | Overall (n = 1115) |
|---|---|
| Type of Bicuspid | |
| No Raphe (type 0) | 11.2% |
| Calcified Raphe (type 1) | 46.5% |
| Non-calcified Raphe (type 1) | 42.3% |
| Calcification Volume in Leaflet ($mm^3$) | 381 (190 – 691) |
| Aortopathy (diameter ≥ 40 mm) | 45.7% |
| Transfemoral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

% or median (IQR)



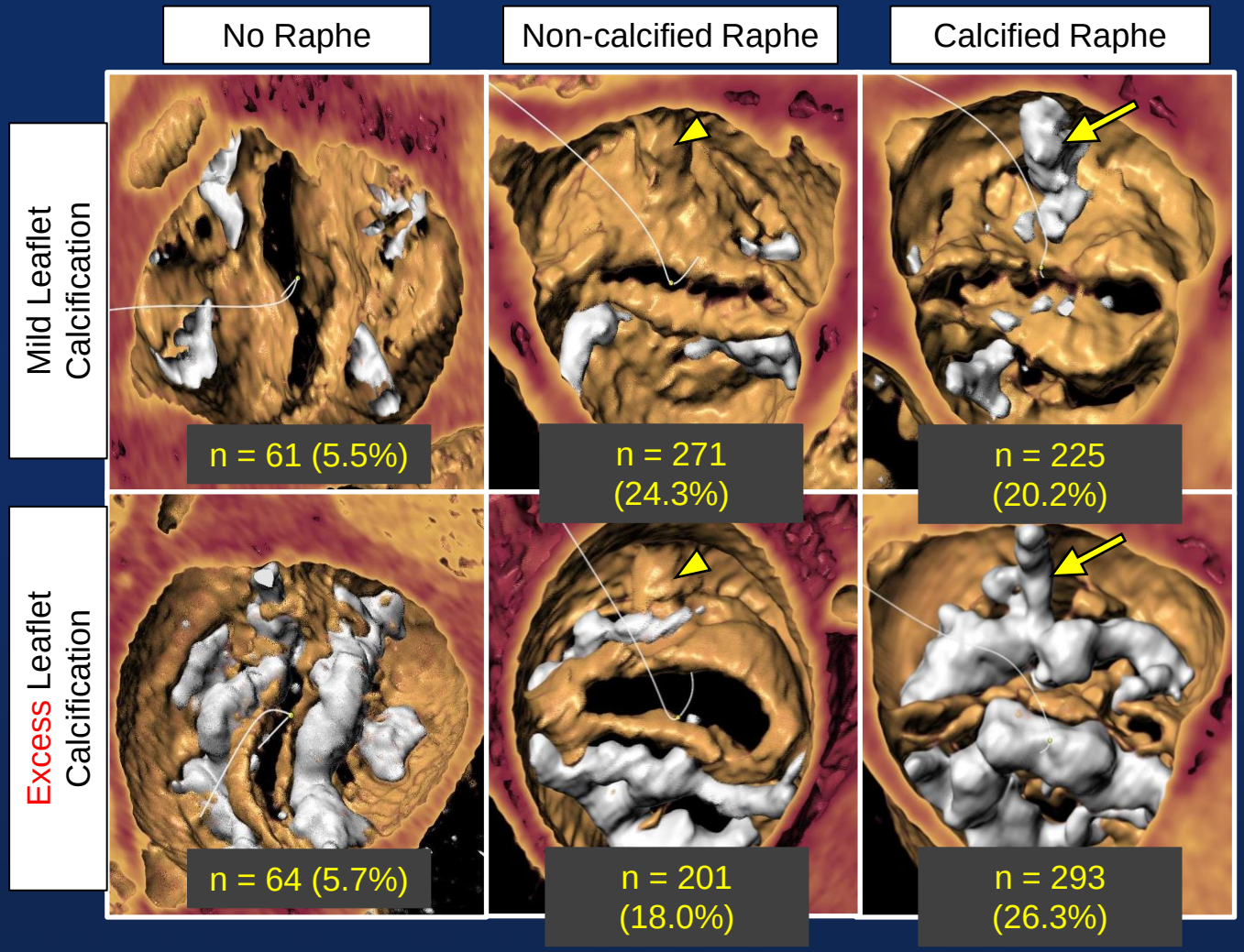
SH Yoon and Raj R. Makkar, Euro PCR 2019

# Various BAV Morphology



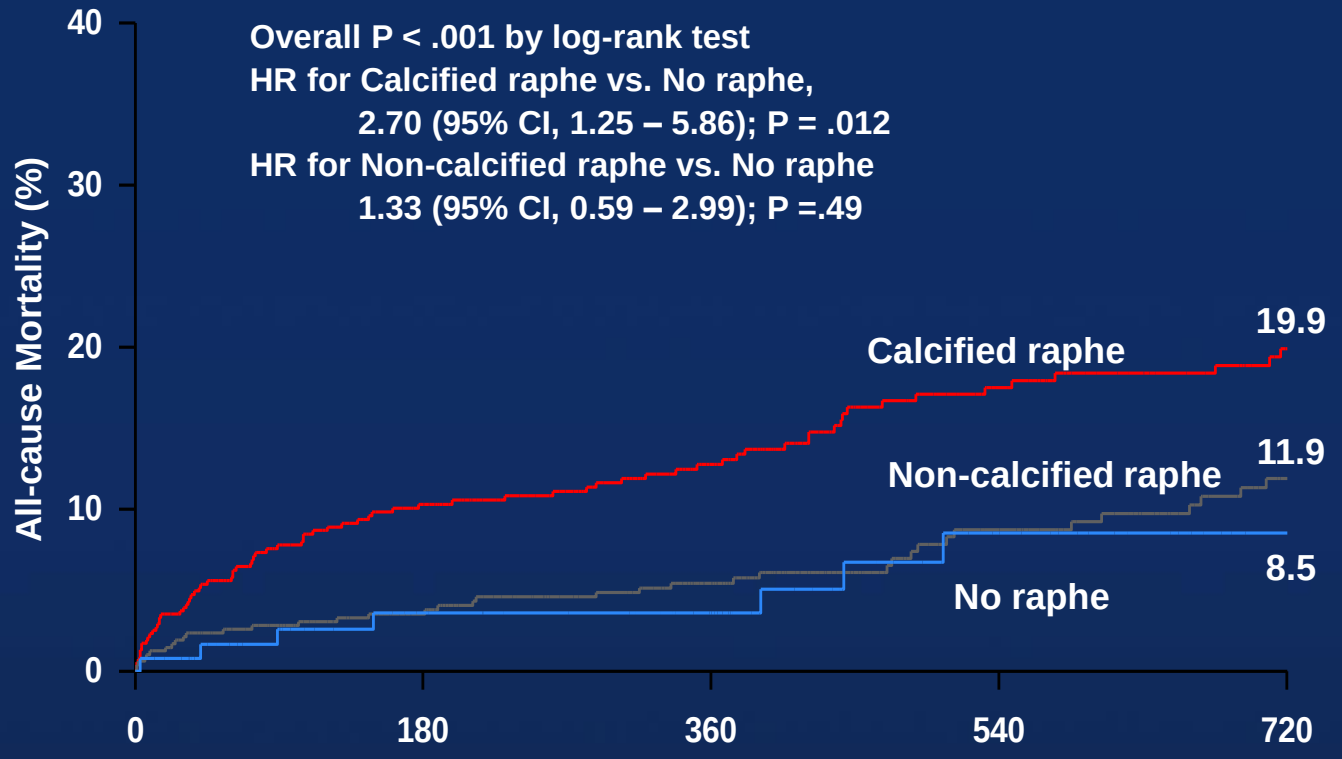

SH Yoon and Raj R. Makkar, Euro PCR 2019

# Phenotype Distribution




SH Yoon and Raj R. Makkar, Euro PCR 2019

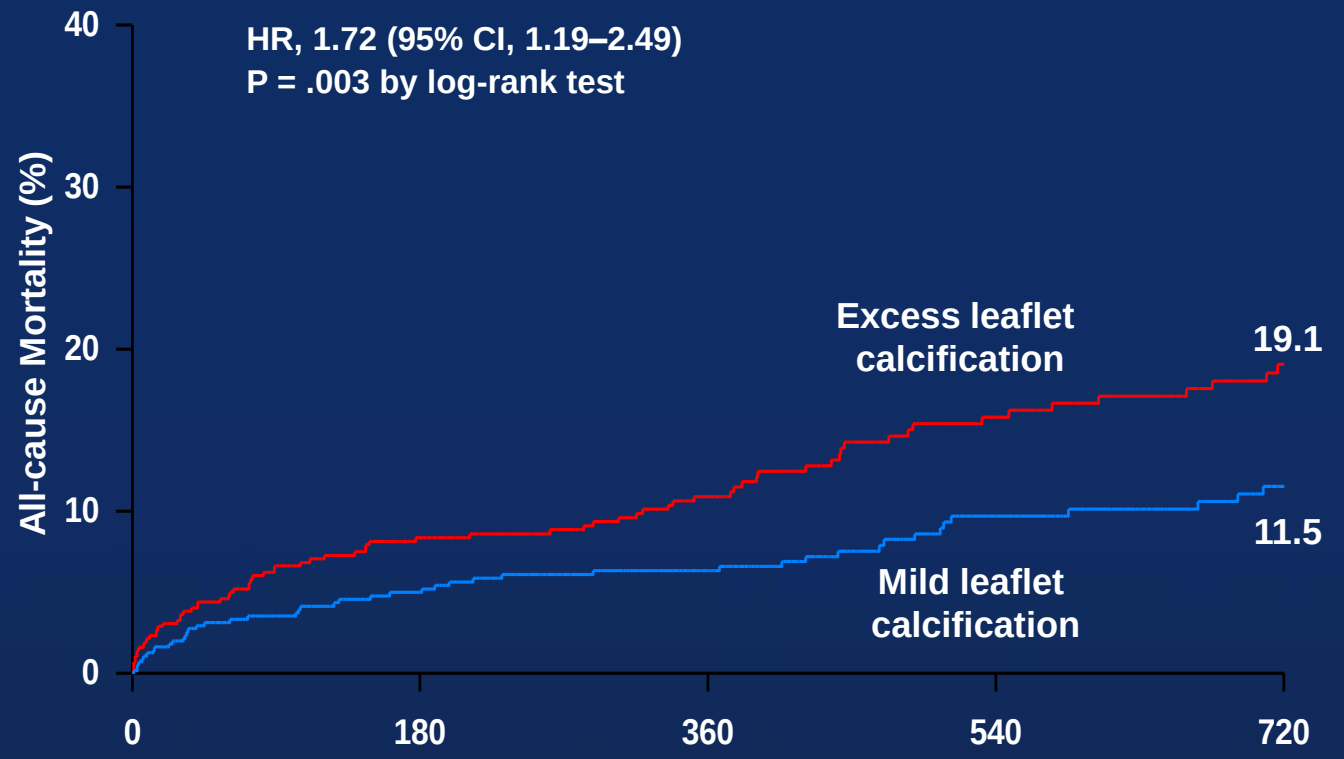
# All-cause Death According to Raphe




| 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

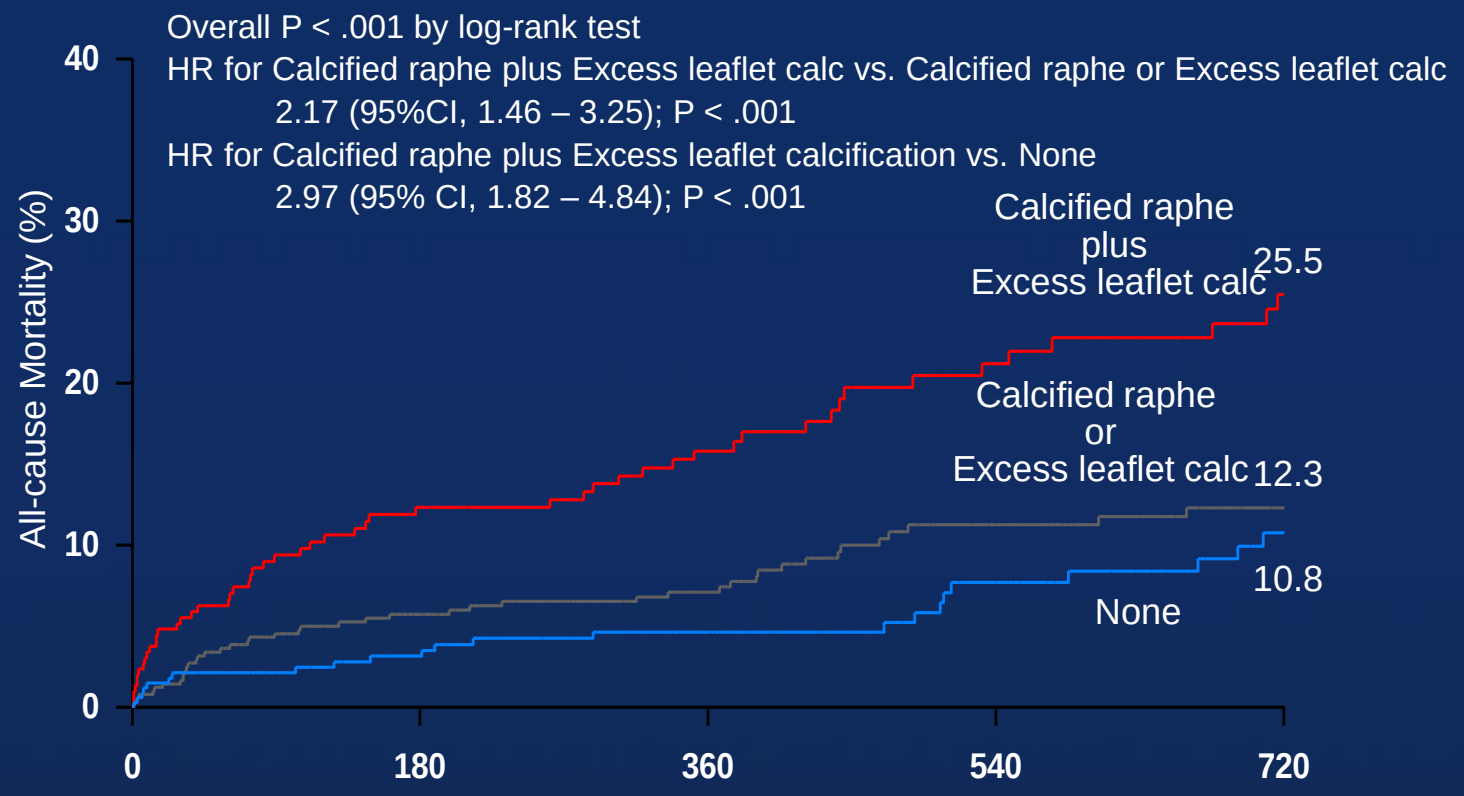
| | HR (95% CI) | *P* Value |
|---|---|---|
| STS score | 1.04 (1.01 – 1.08) | 0.02 |
| MR ≥ moderate at baseline | 1.65 (1.02 – 2.68) | 0.04 |
| Type of Bicuspid AV | | 0.001 |
| No raphe (Sievers' type 0) | Reference | – |
| Non-calcified raphe (Sievers' type 1) | 1.55 (0.69 – 3.50) | 0.29 |
| Calcified 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

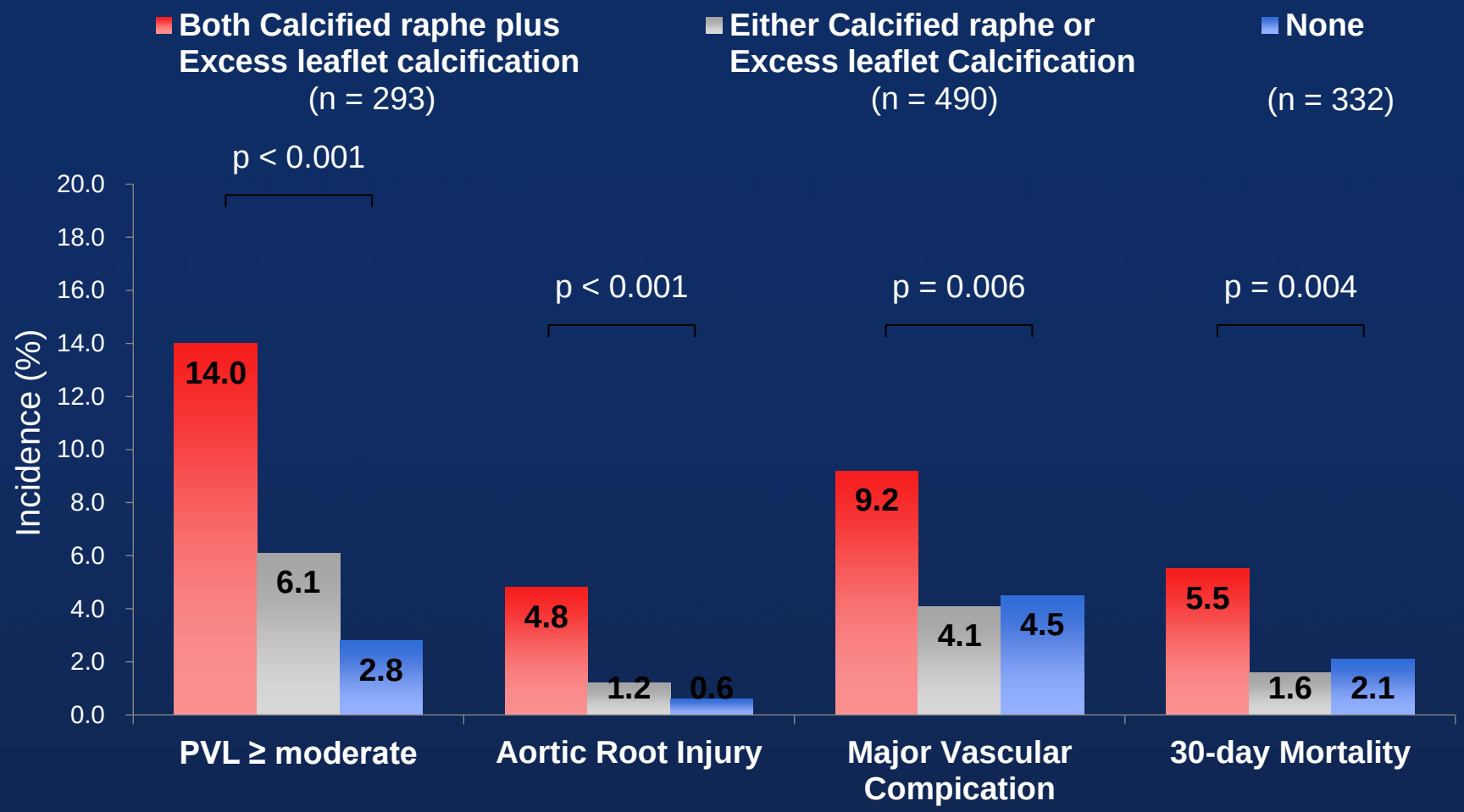
## 1115 Bicuspid AS patients, 25 Centers




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

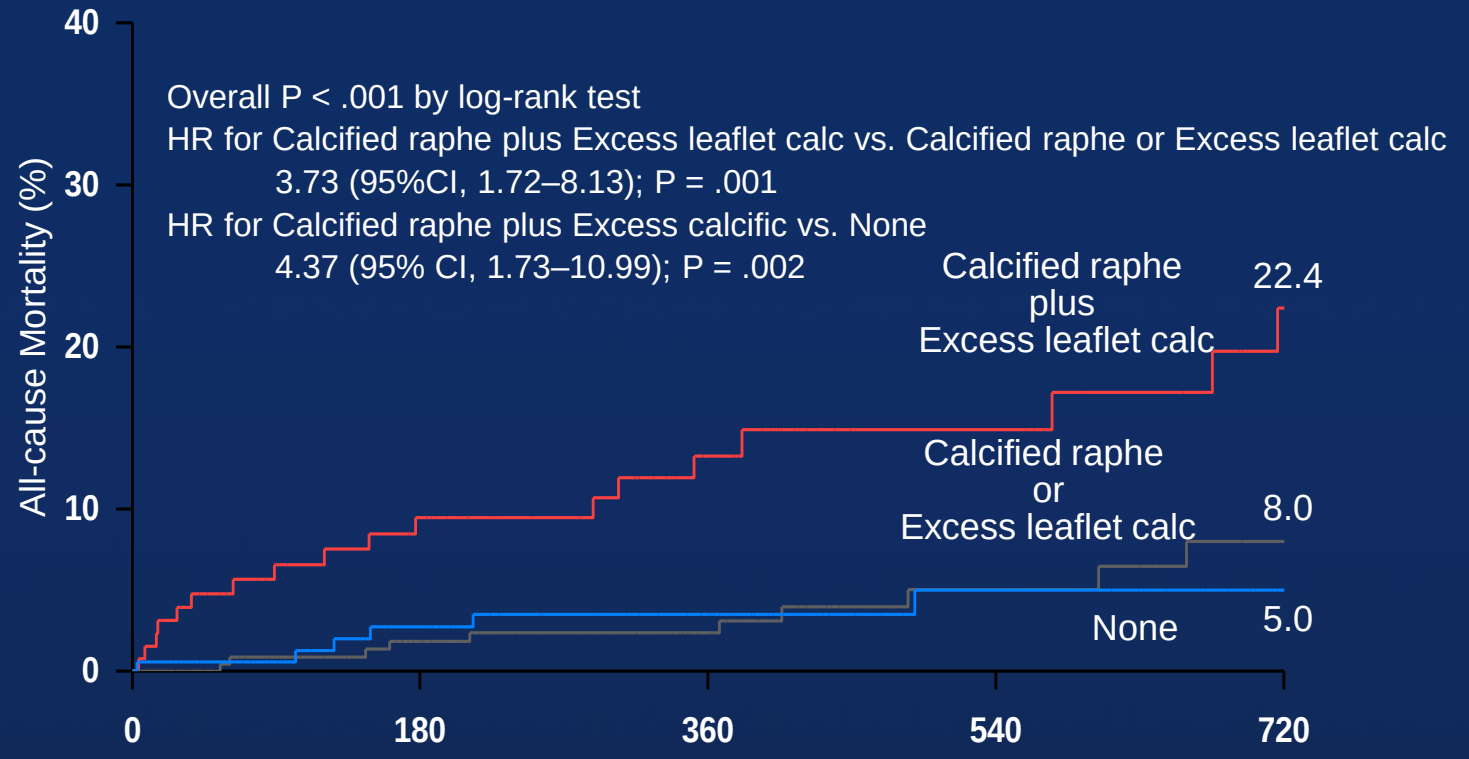
**SH Yoon and Raj R. Makkar, Euro PCR 2019**

# 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

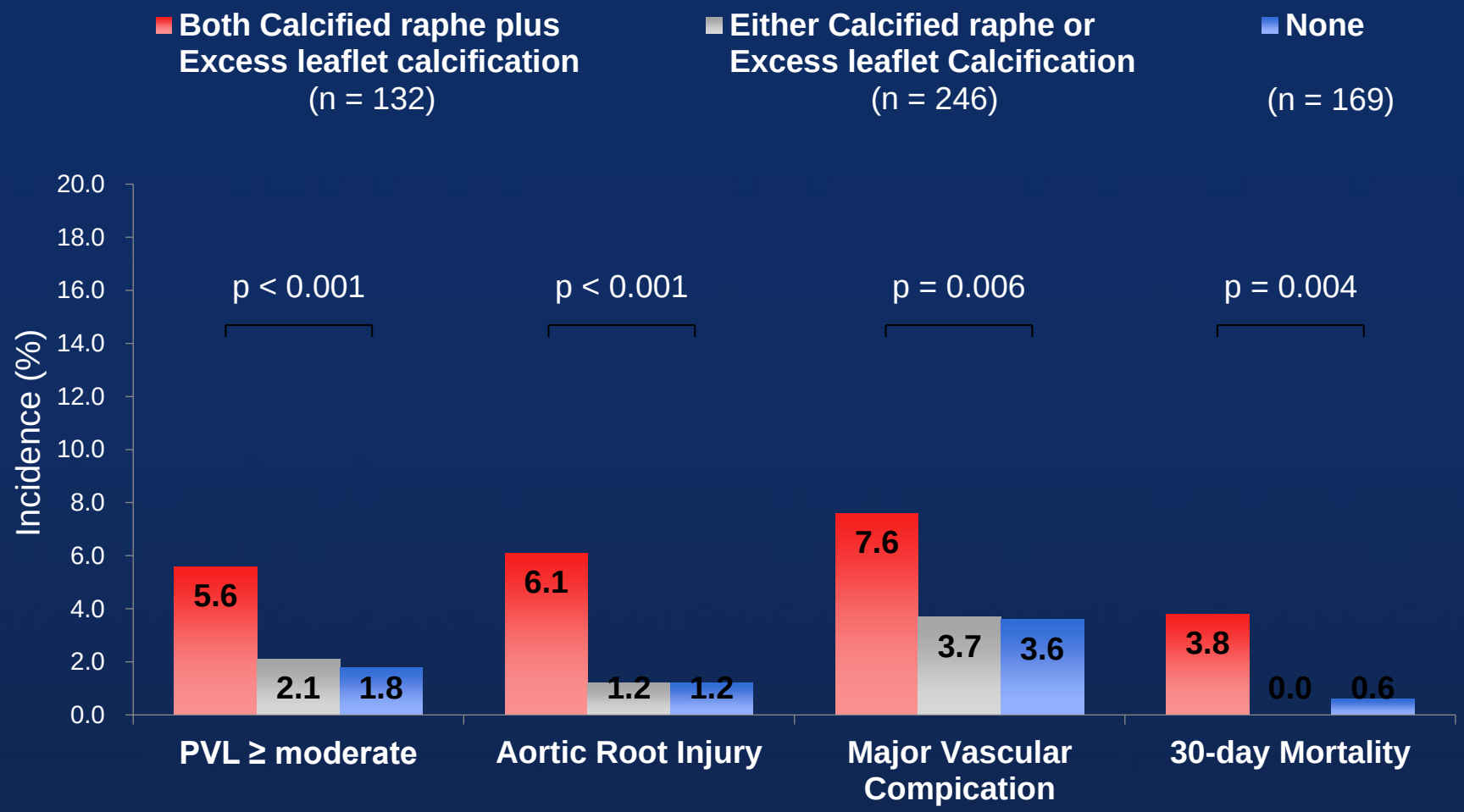



| No. at Risk | | | |
|---|---|---|---|
| Ca-raphe plus excess calc | 132 | 61 | 28 |
| Ca-raphe or excess calc | 246 | 143 | 54 |
| None | 169 | 102 | 40 |



SH Yoon and Raj R. Makkar, Euro PCR 2019

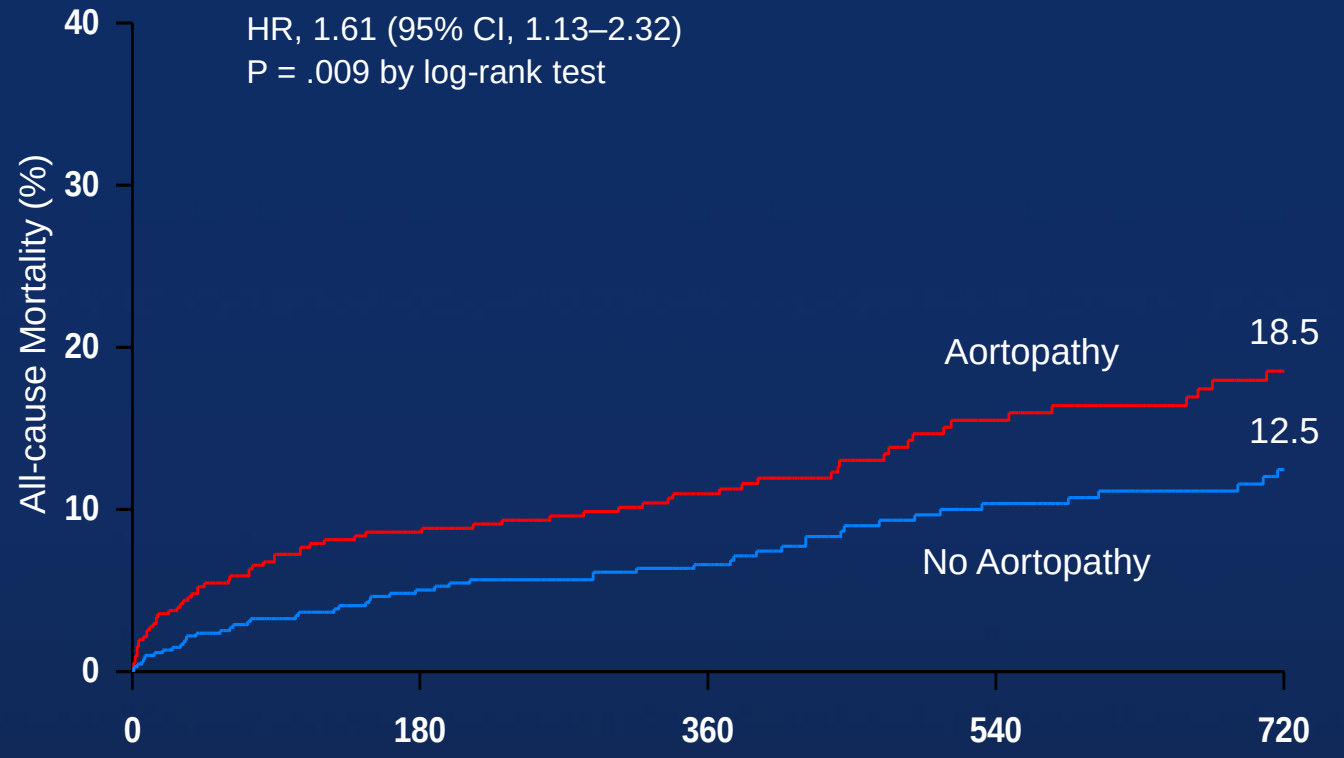
# Outcomes According to BAV Phenotype
# Among Low-Risk Patients with New Devices






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

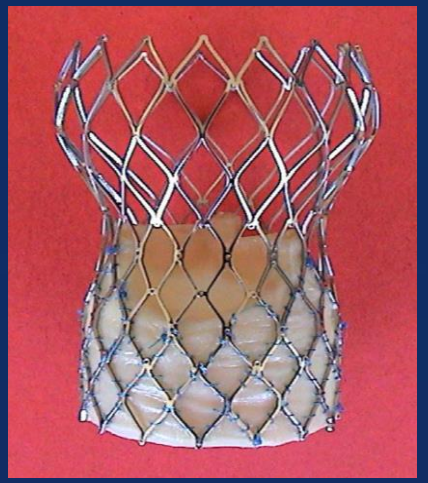
# Optimal TAVR for Bicuspid AV

- 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.

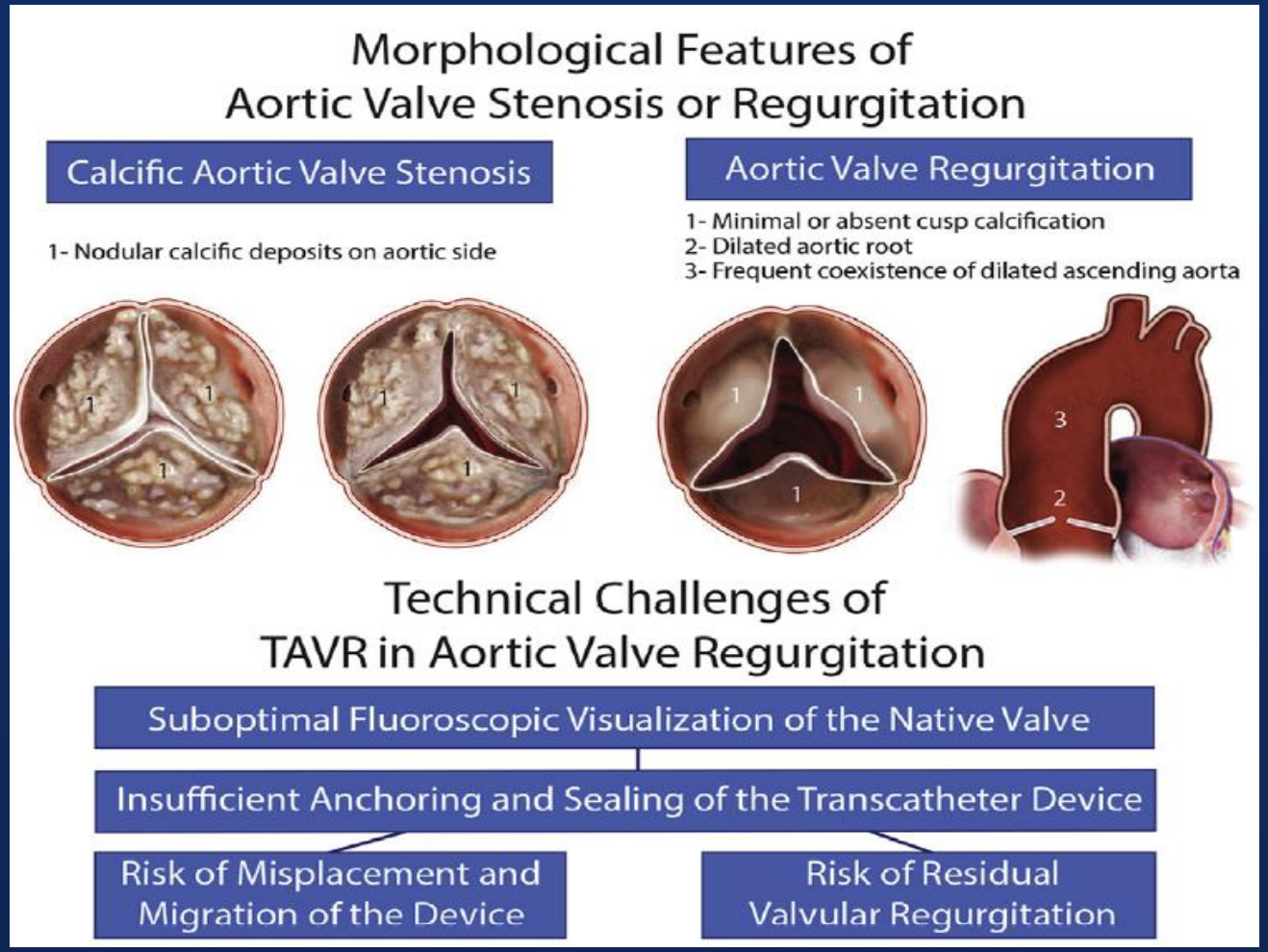
# TAVR for AR

# 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**

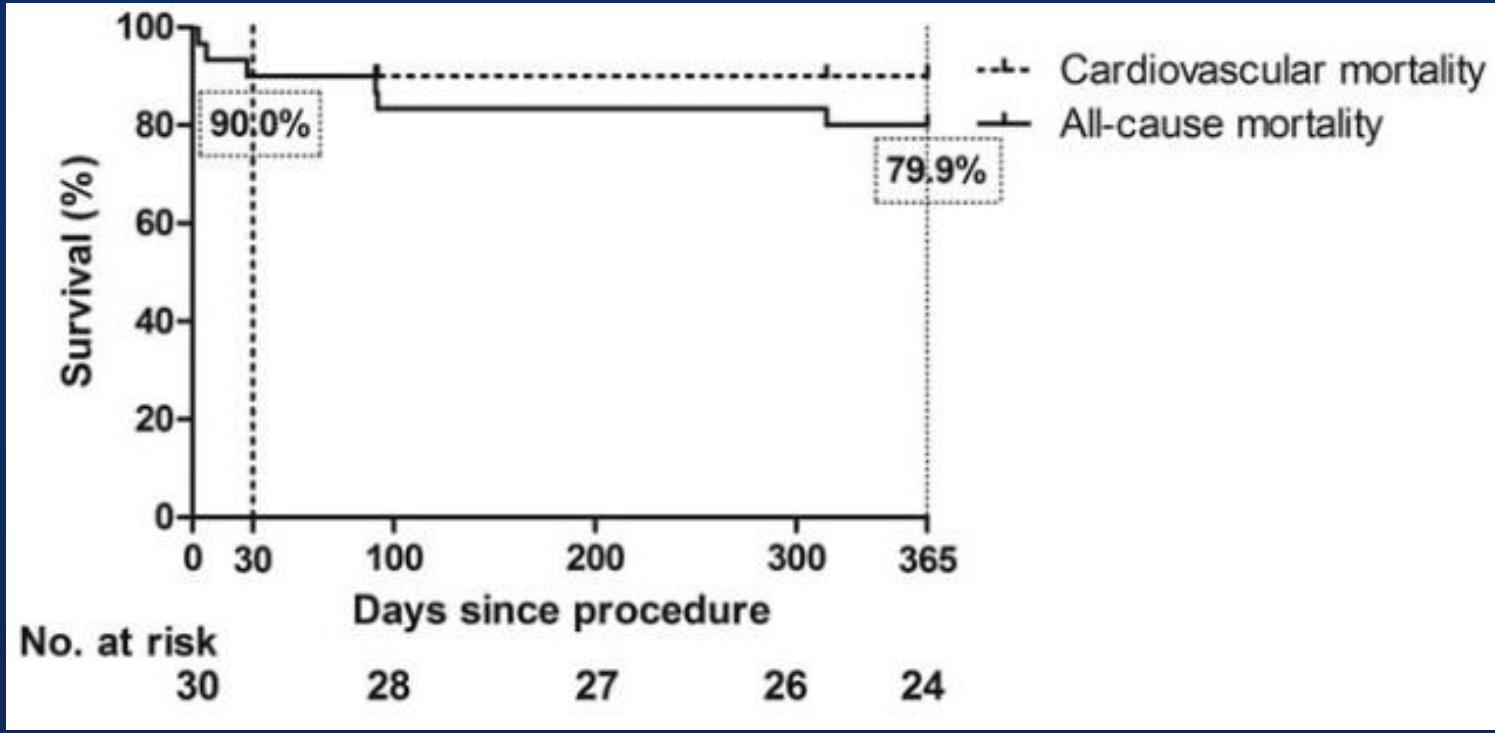
| | |
|---|---|
| Myocardial infarction | 0 |
| Cerebrovascular event | 0 |
| Bleeding, major or life-threatening | 3 (9.7) |
| Access site complication | |
| Minor | 1 (3.2) |
| Major | 3 (9.7) |
| Acute kidney injury | |
| Stage 1 or 2 | 6 (19.3) |
| Stage 3 | 1 (3.2) |
| Permanent pacemaker implantation | 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

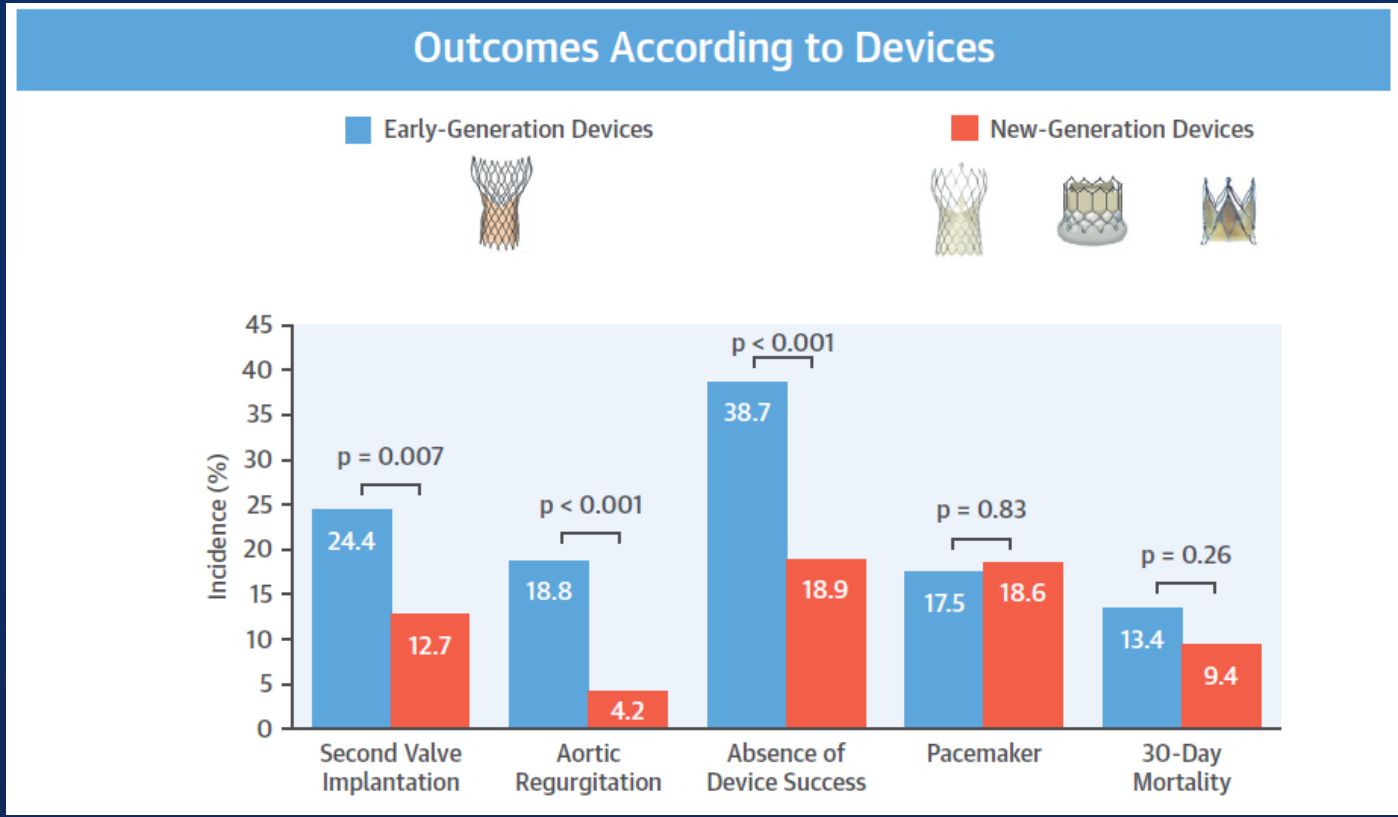
**Pure native AR TAVR multicenter registry, total 331 patients, STS score 6.7 ±6.7**

| | 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**

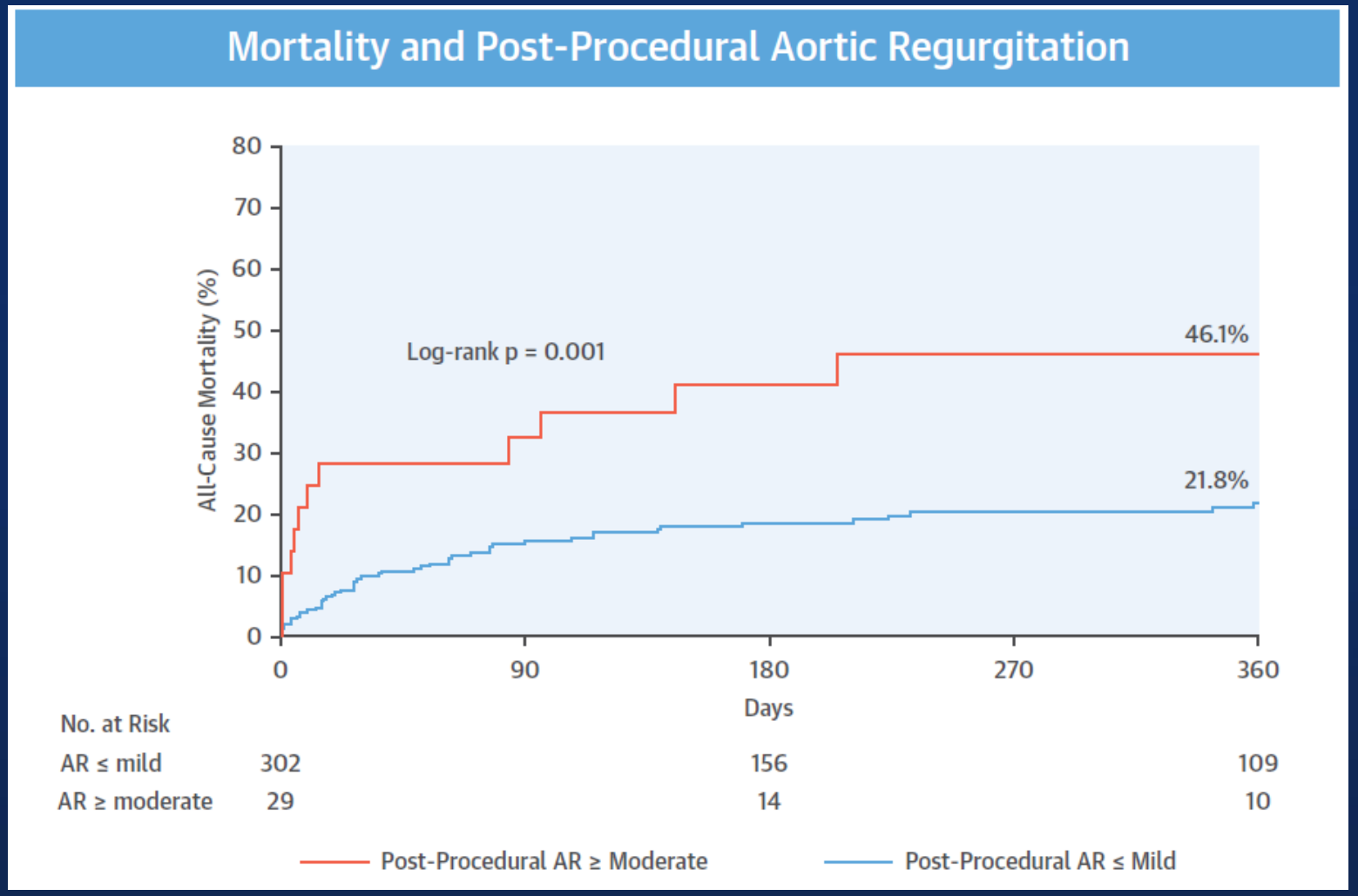



Implications: High-risk or inoperable patients who undergo TAVR to treat pure native AR fare better when they receive new- vs early-generation valves.

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%) |

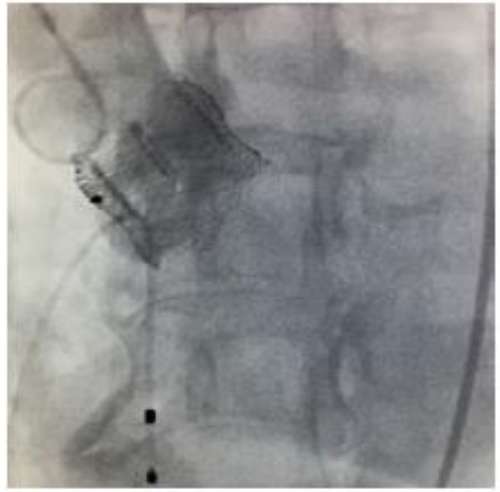


Fadi J. Sawaya, et al. JACC intv 2017

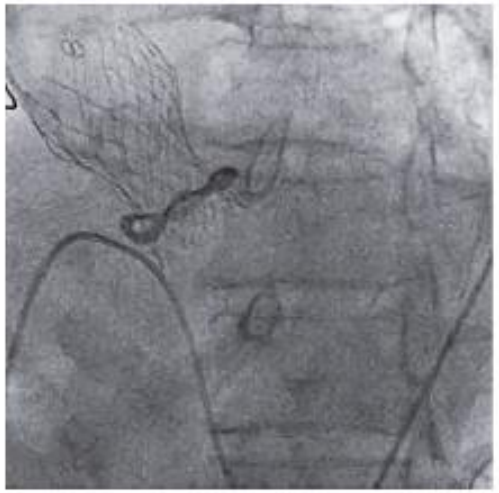
# Pure AR in native and prosthetic valve

**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

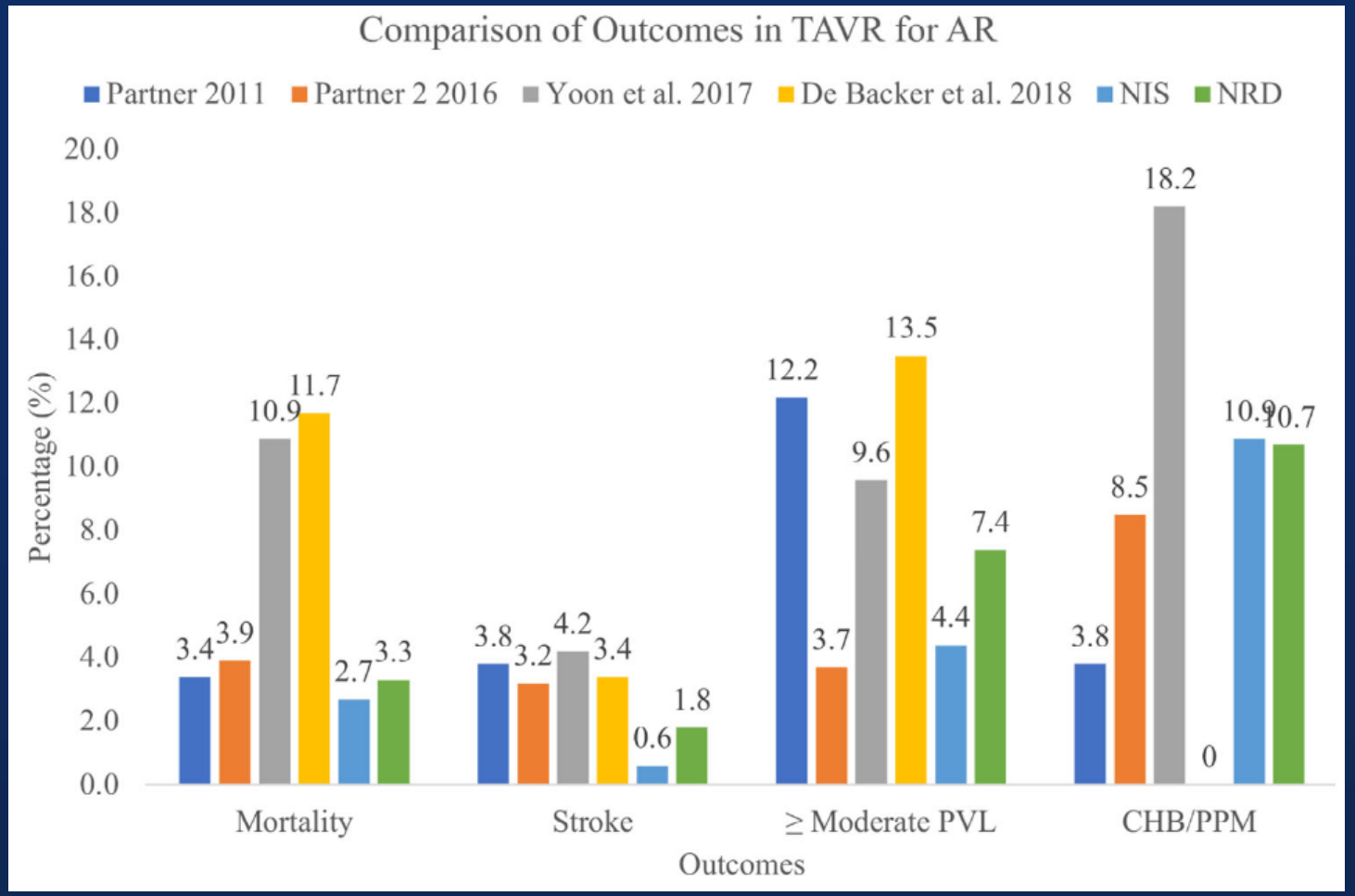
**TABLE 2** Complications associated with TAVR in AR

| 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

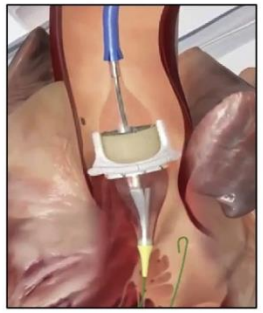
# TAVR

## Valve-in-Valve

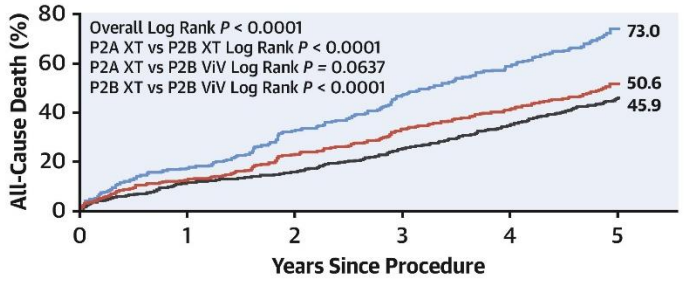
# PARTNER 2 Valve-in-Valve Registry

## 5-year outcomes

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



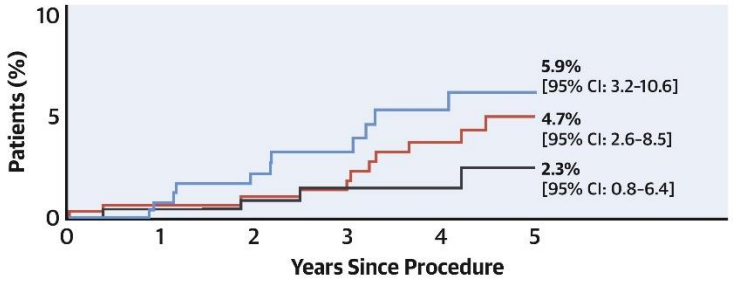
A




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

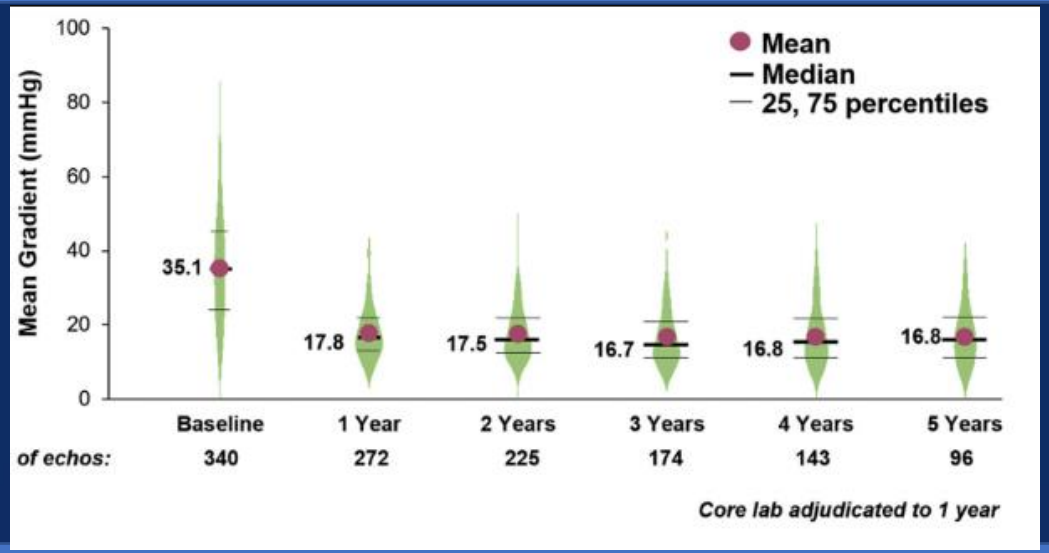



No. at risk:

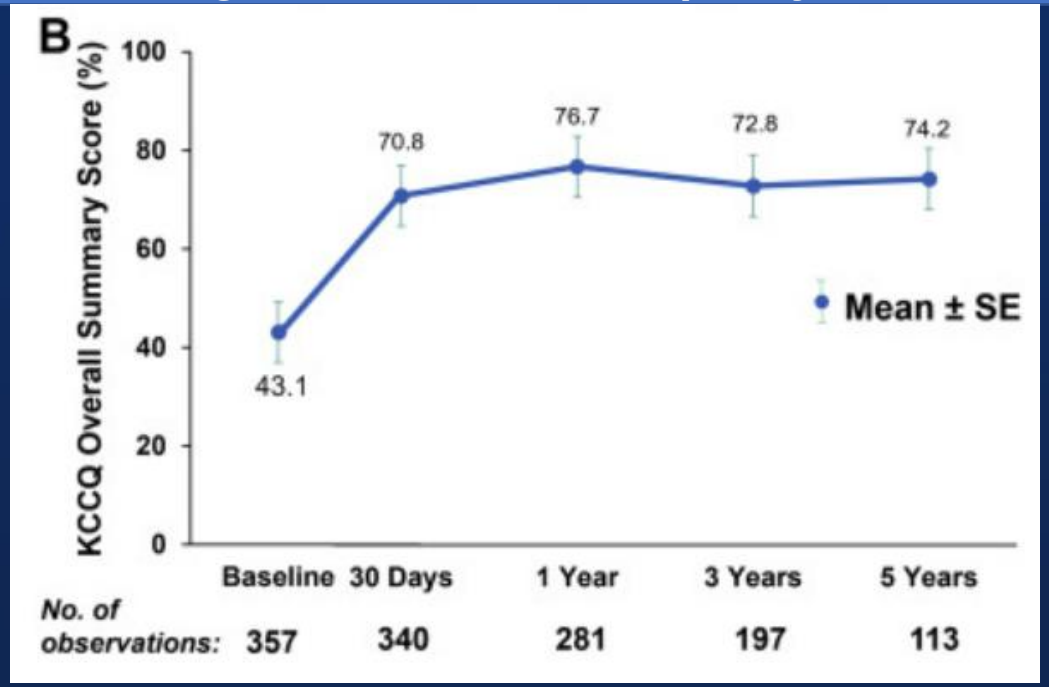
| | | | | | | |
|---|---|---|---|---|---|---|
| SVD-Related HVD | 273 | 251 | 201 | 158 | 125 | 86 |
| All BVF | 365 | 319 | 272 | 231 | 185 | 137 |
| SVD-Related BVF | 273 | 253 | 205 | 162 | 131 | 92 |

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

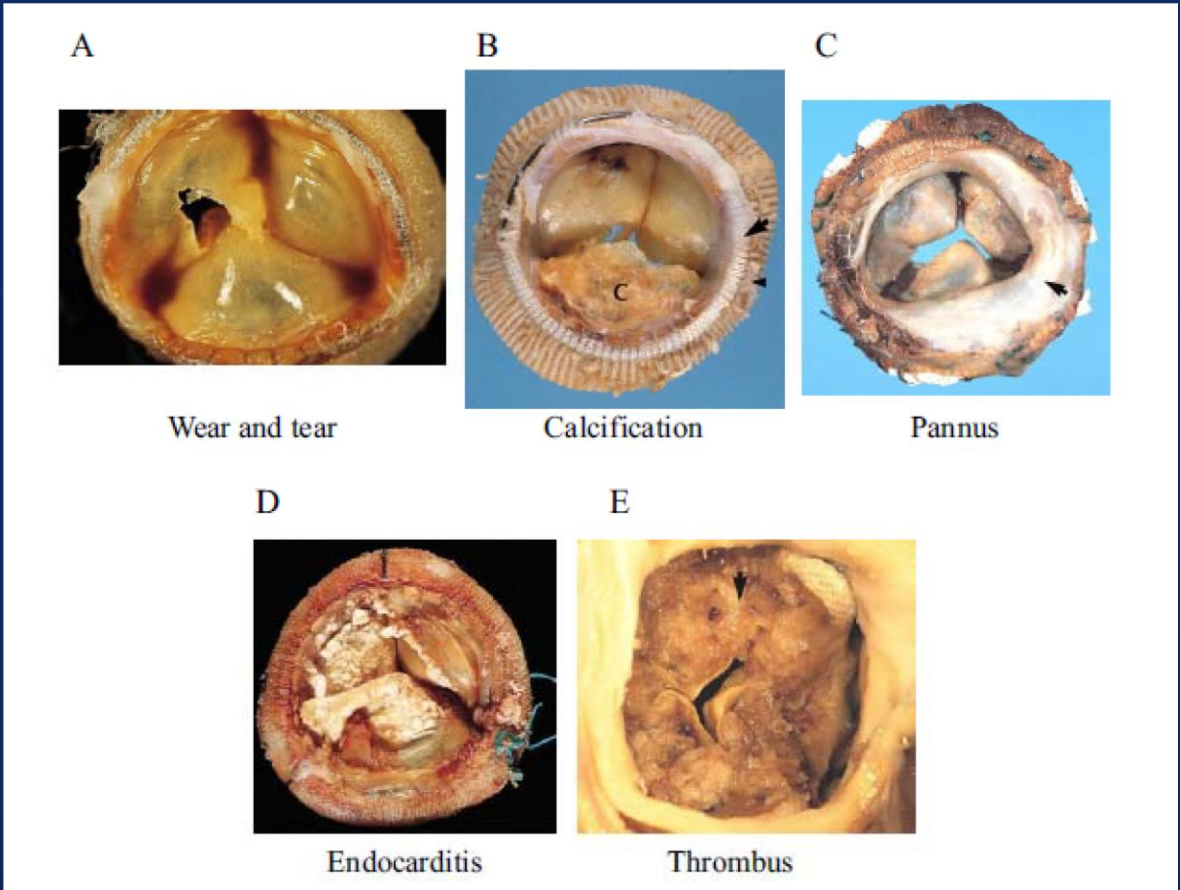
Prospective longitudinal study of 137 patients who had previously undergone bioprosthetic valve surgery.

- 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

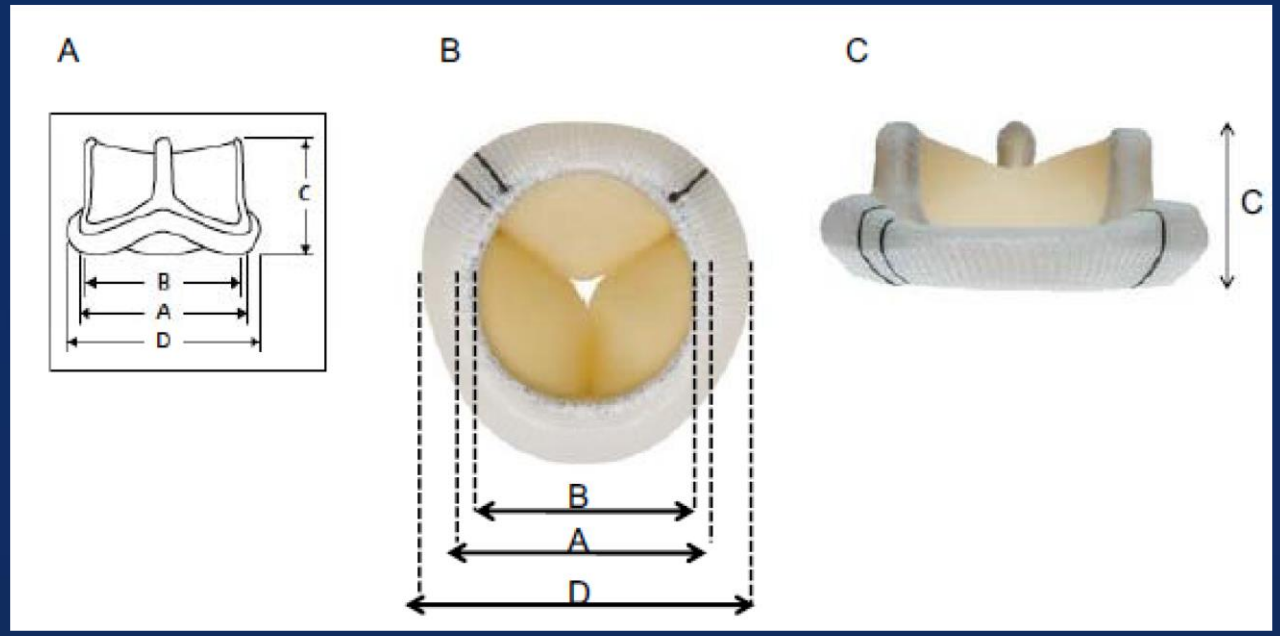
(D) Endocarditis

(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.





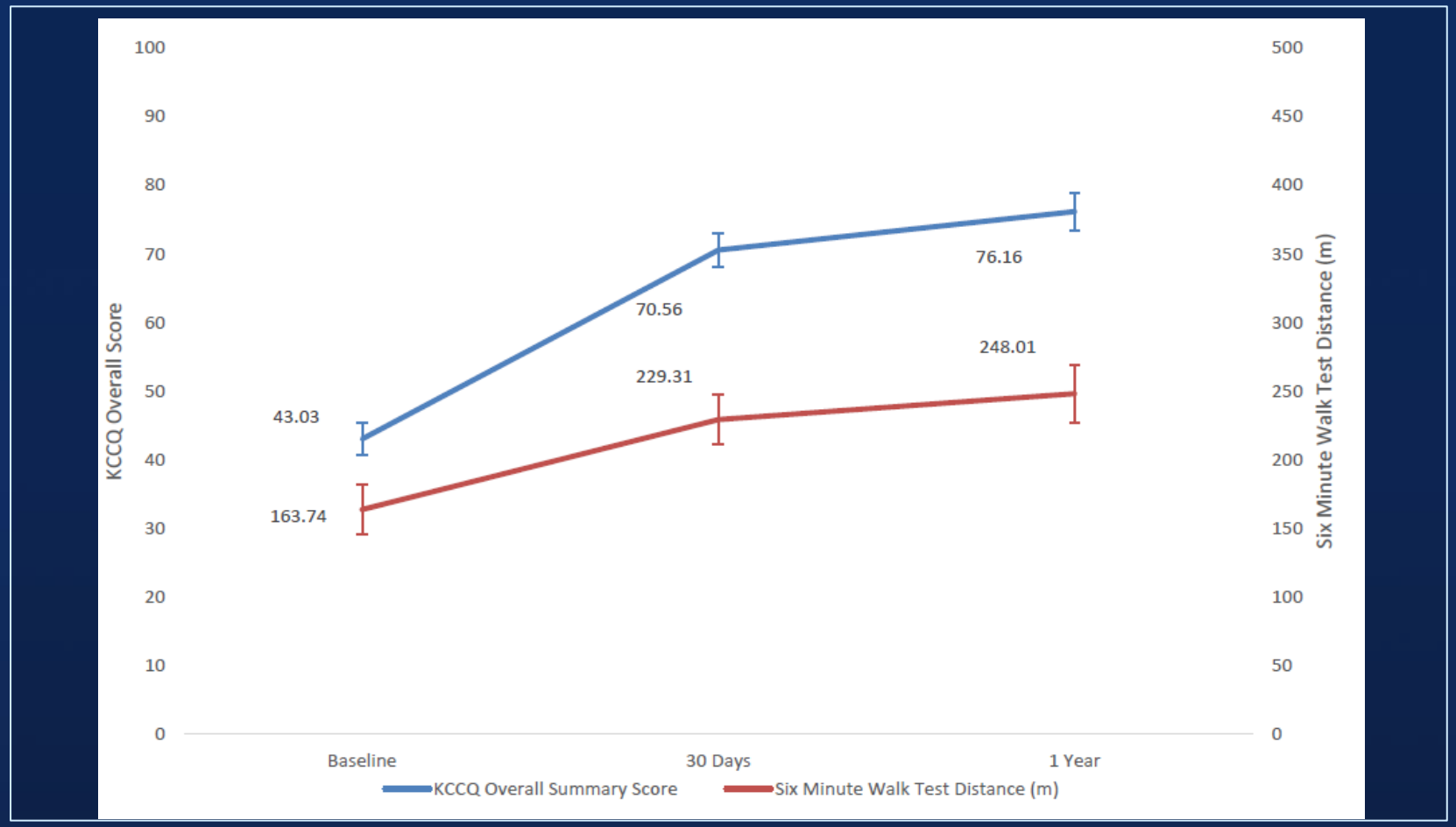
Piazza, N, et al. JACC Cardiovasc Interv. 2011;4:721-32.

# 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

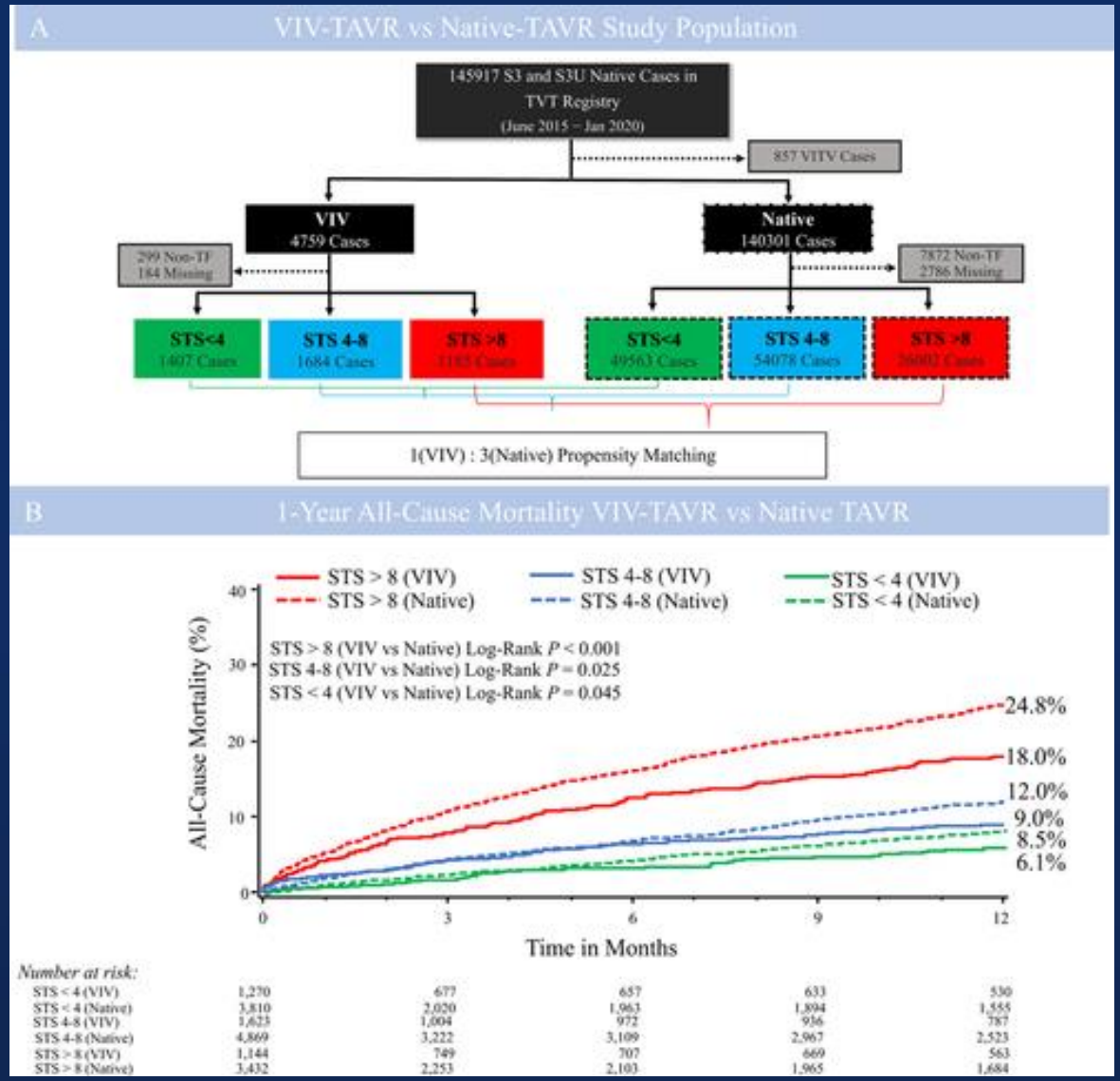
## Valve-in-Valve Registry

| 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

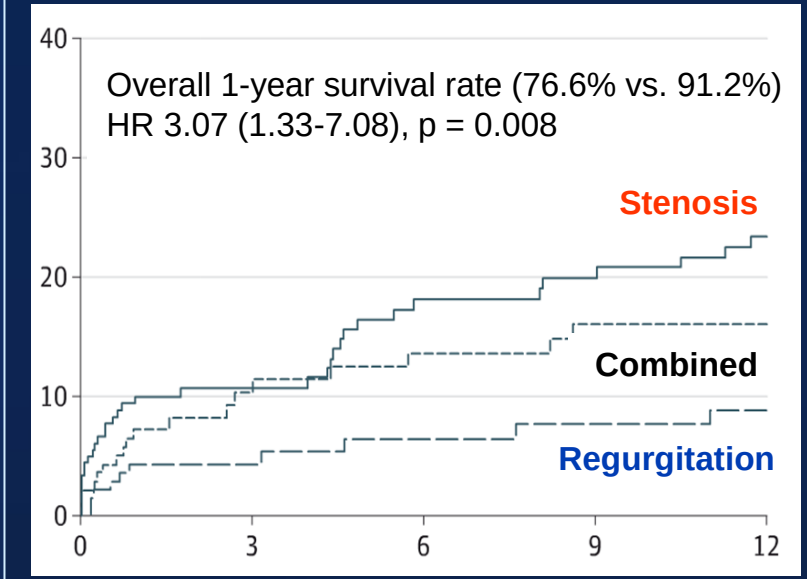
# Valve-In Valve TAVR



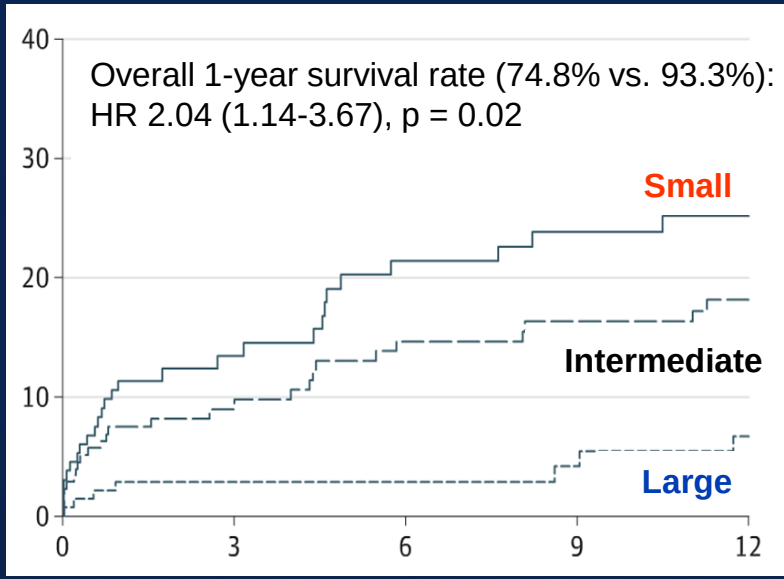

Kaneko T, et al., Circ Cardiovasc Interv. 2021 May;14(5)

# 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 |

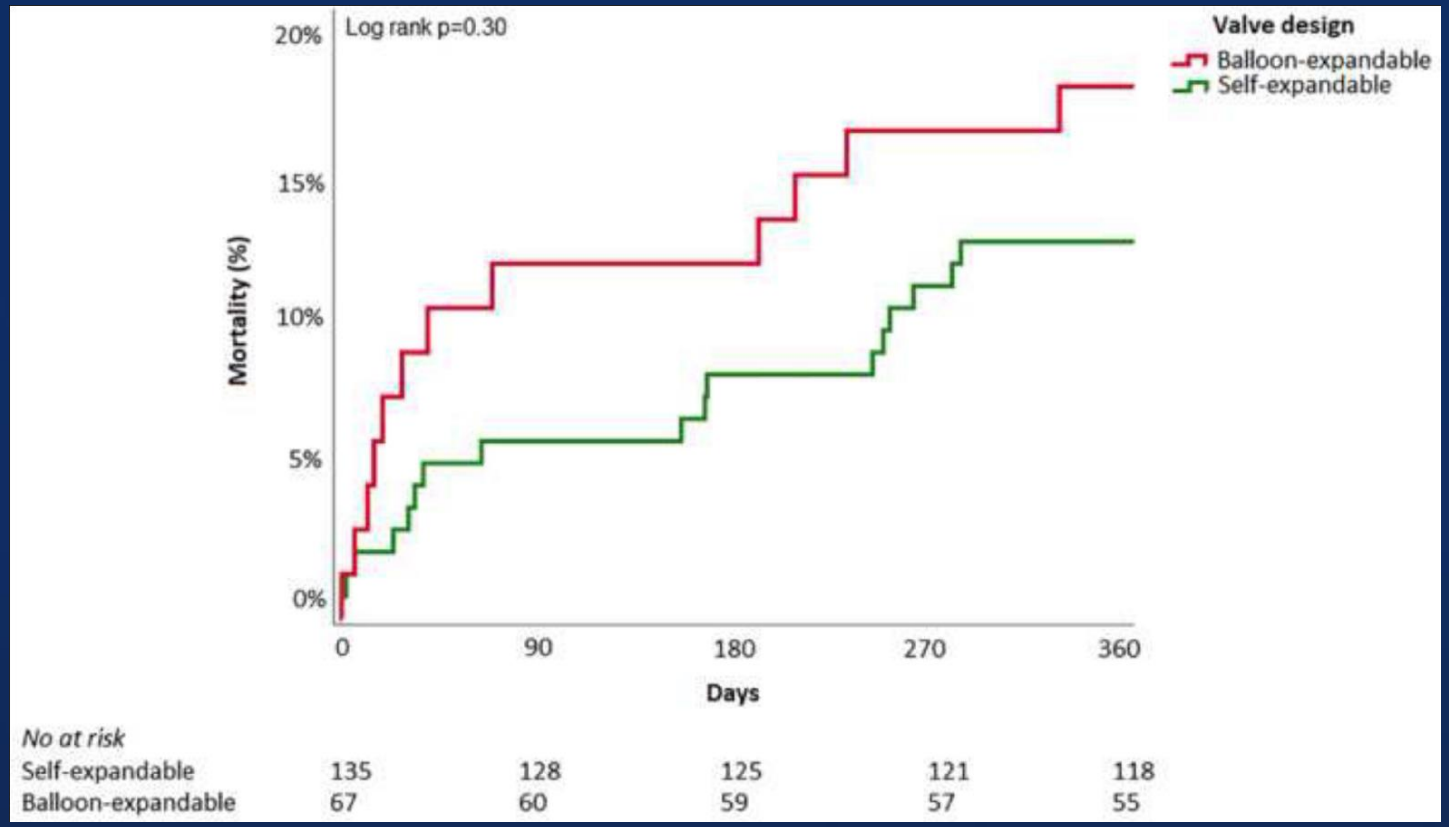
# 1-year Outcomes of Valve-in-Valve

## 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 |

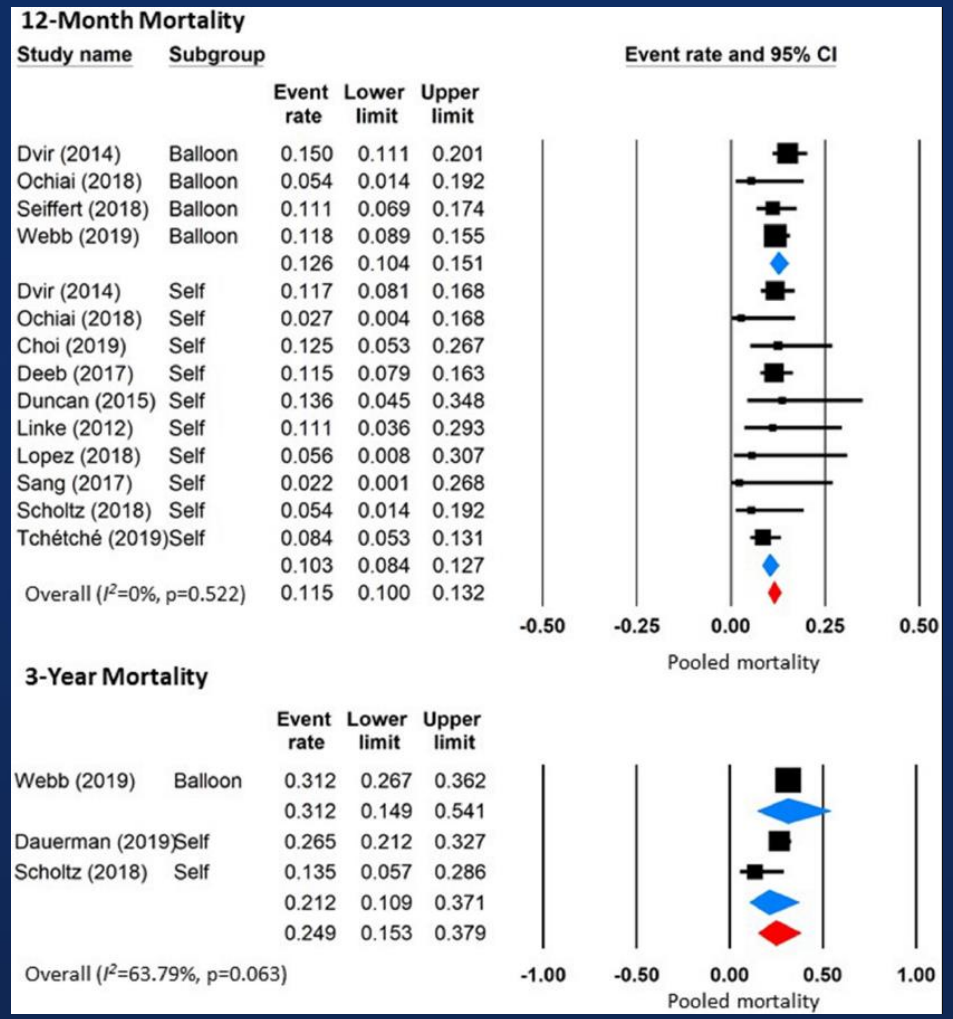
* p value < 0.05

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




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

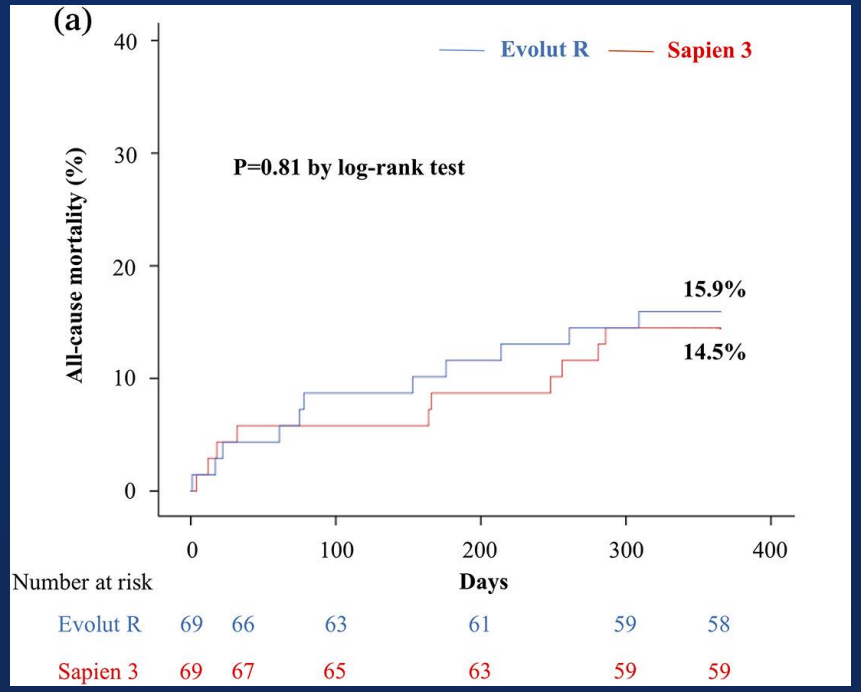
# Balloon-expandable vs. Self-expandable outcome in Valve-in-Valve




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

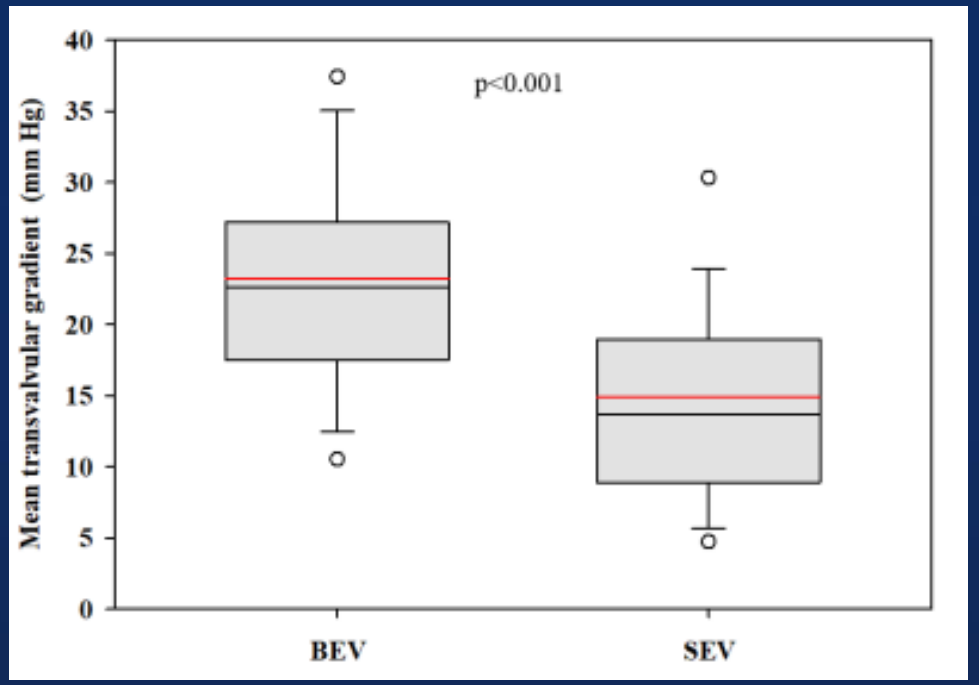
# Balloon-expandable vs. Self-expandable In small aortic annulus (≤23mm)

## 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

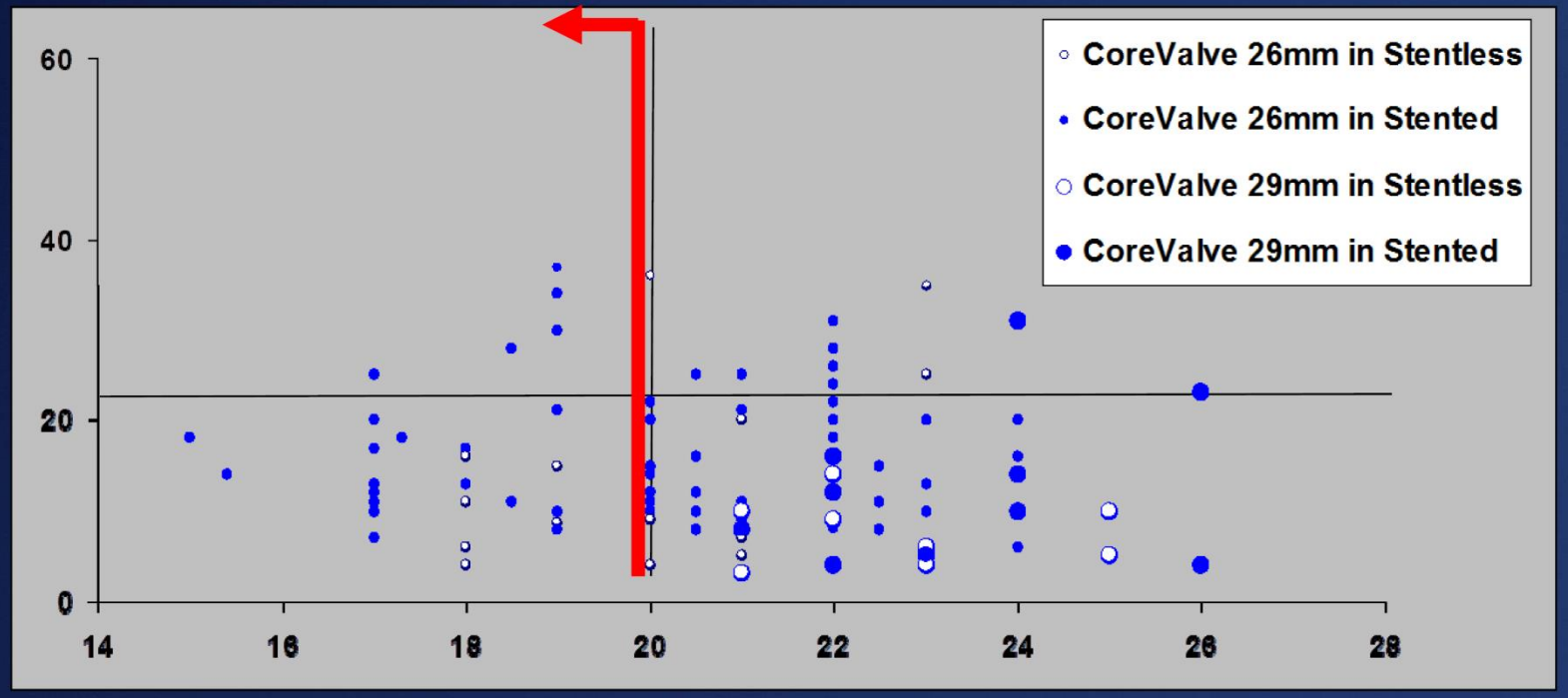



Rodés-Cabau J, et al., The LYTEN Trial. J Am Coll Cardiol. 2022 May 13:S0735-1097(22)04978-6.

# Post Procedural Gradients

## CoreValve Device

### Mean Aortic-Valve Gradients (mmHg)



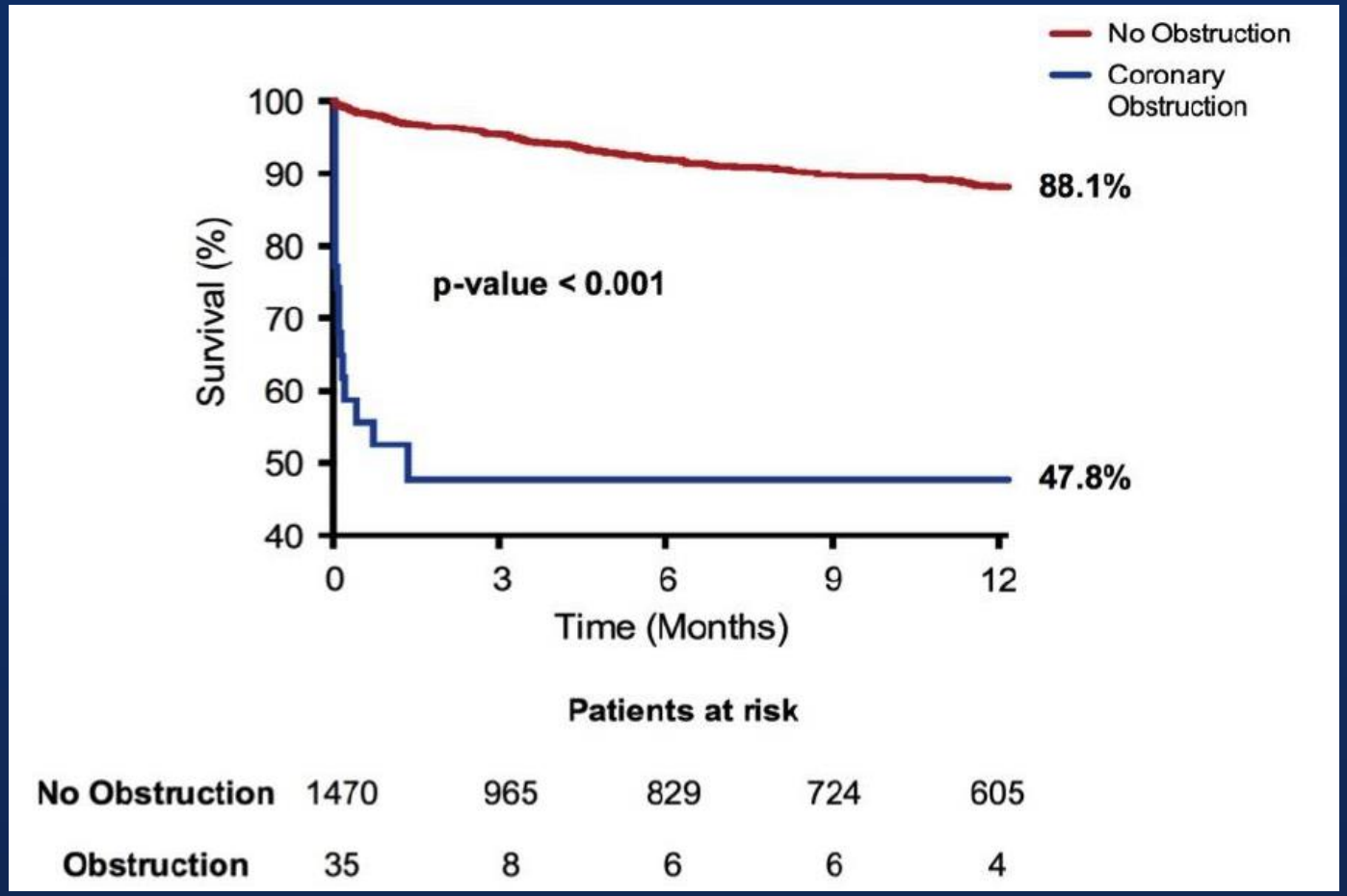

### Surgical Bioprosthesis *Internal* Diameter (mm)

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

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

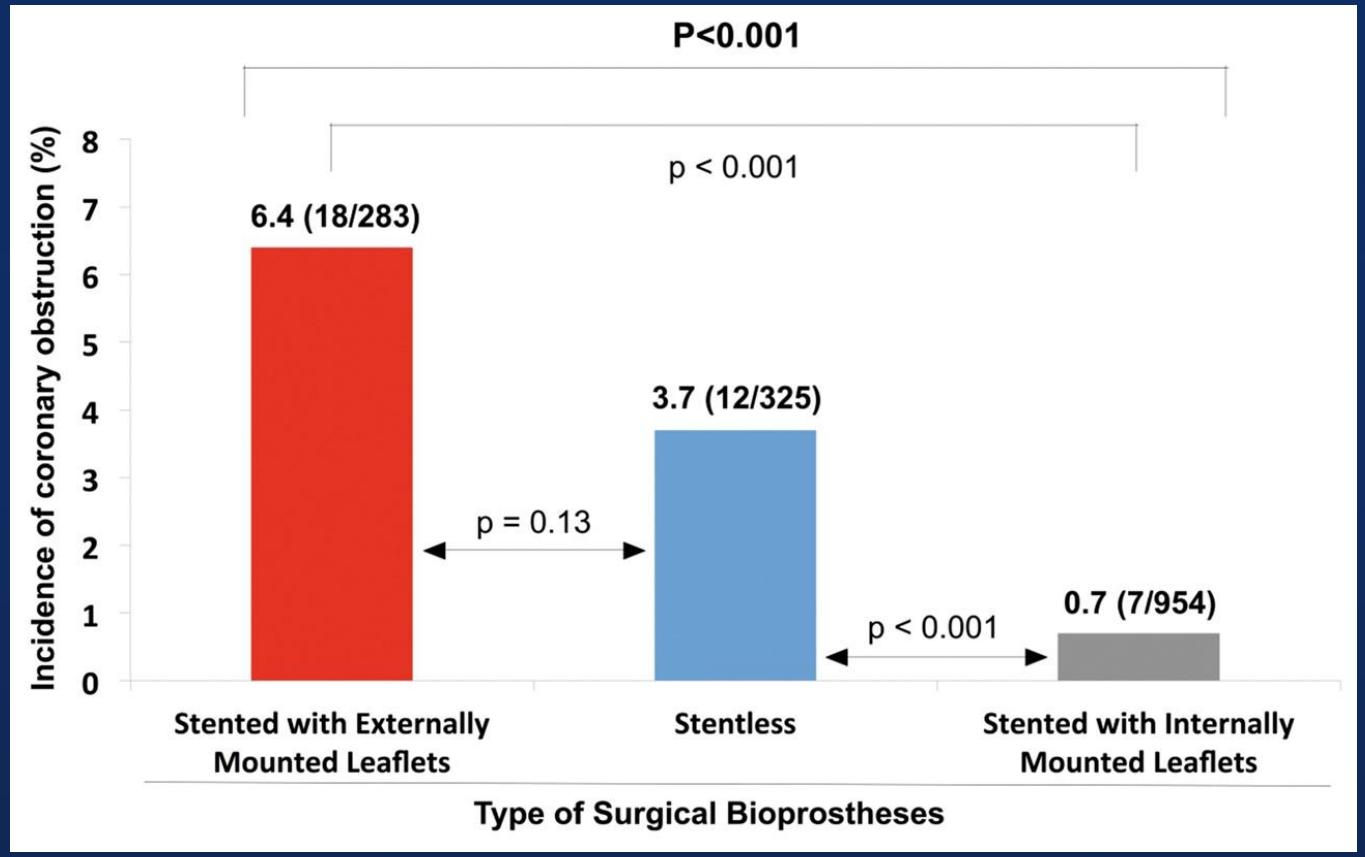
* Mean aortic-valve gradient> 20mmHg.

# Coronary Obstruction after Valve-in-Valve procedure



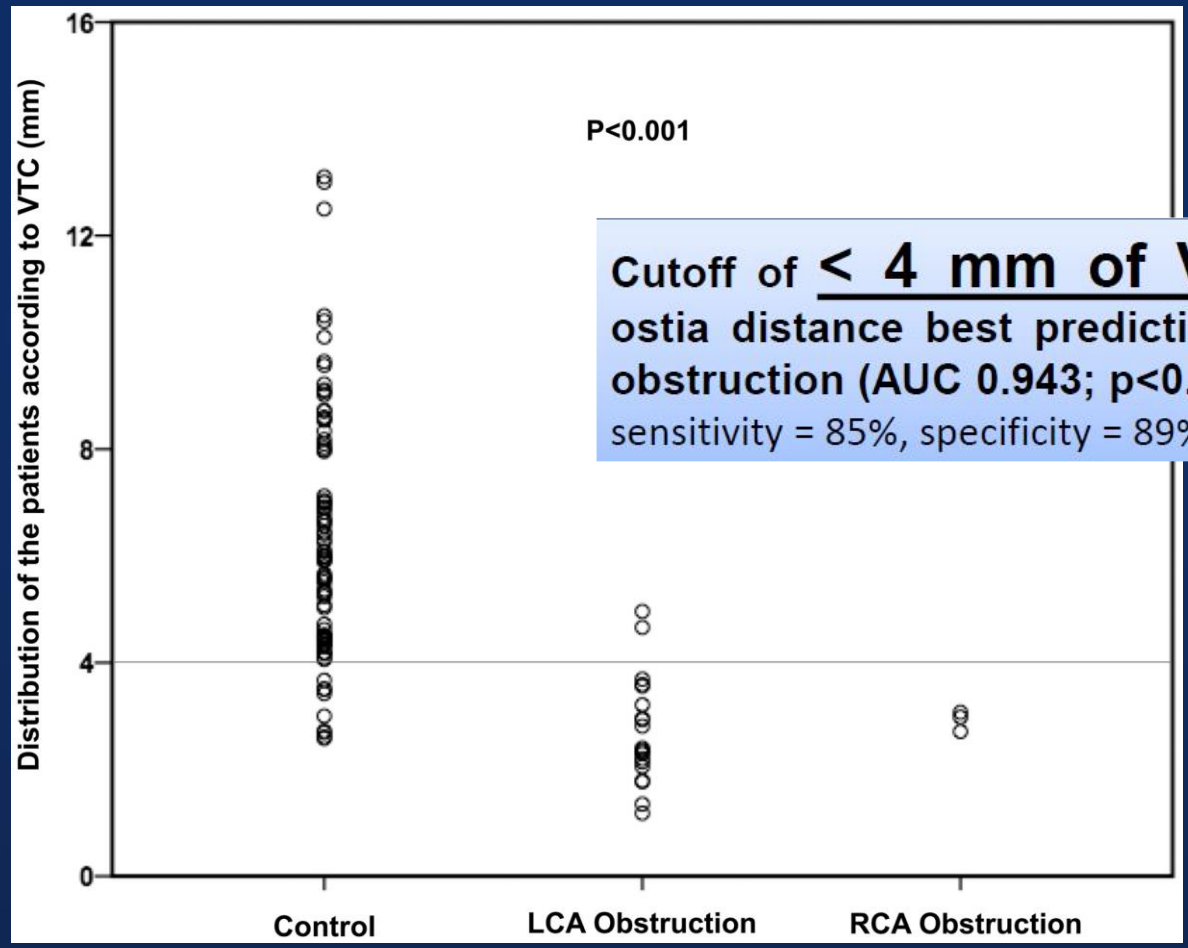

*Ribeiro HB et al. TCT 2016*

# 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)

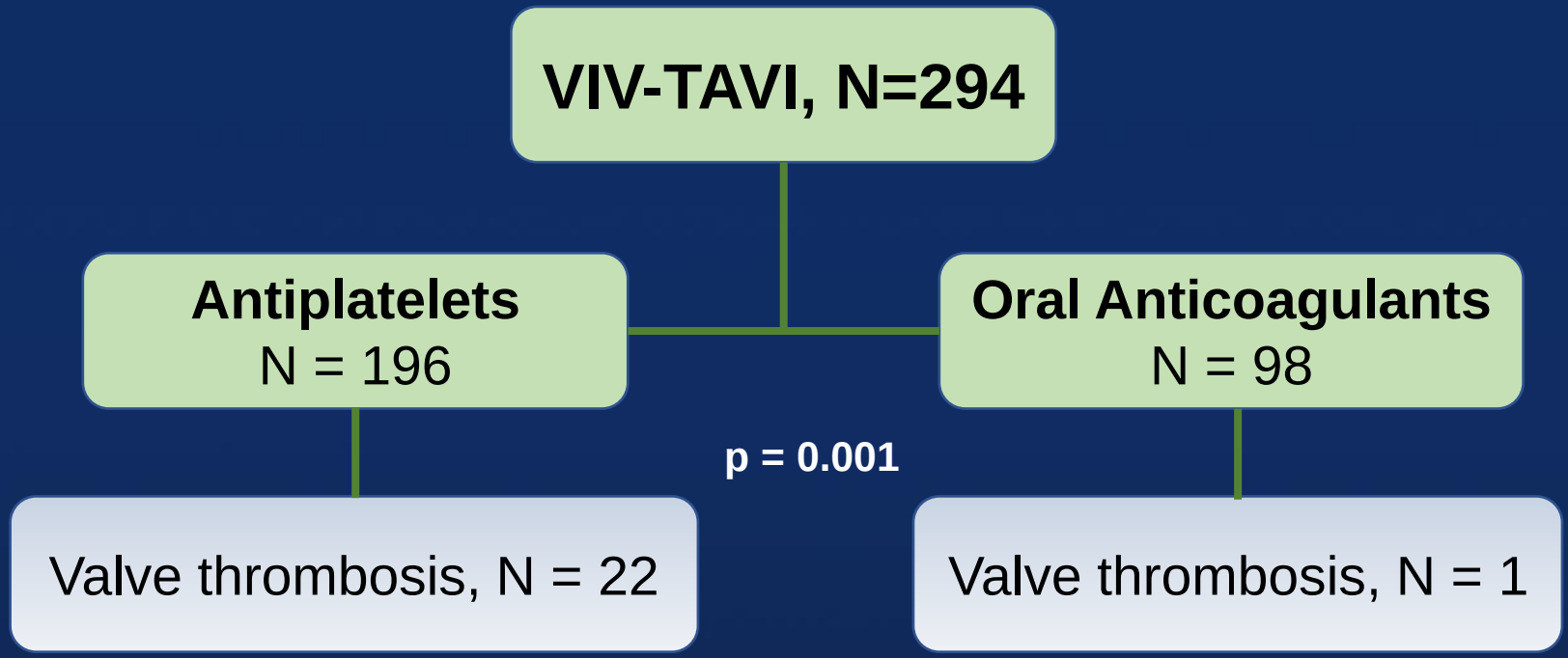



Cutoff of < 4 mm of VTC-LCA ostia distance best predicting coronary obstruction (AUC 0.943; p<0.001)
sensitivity = 85%, specificity = 89%

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

# Thrombosis after aortic VinV

## Incidence of valve thrombosis

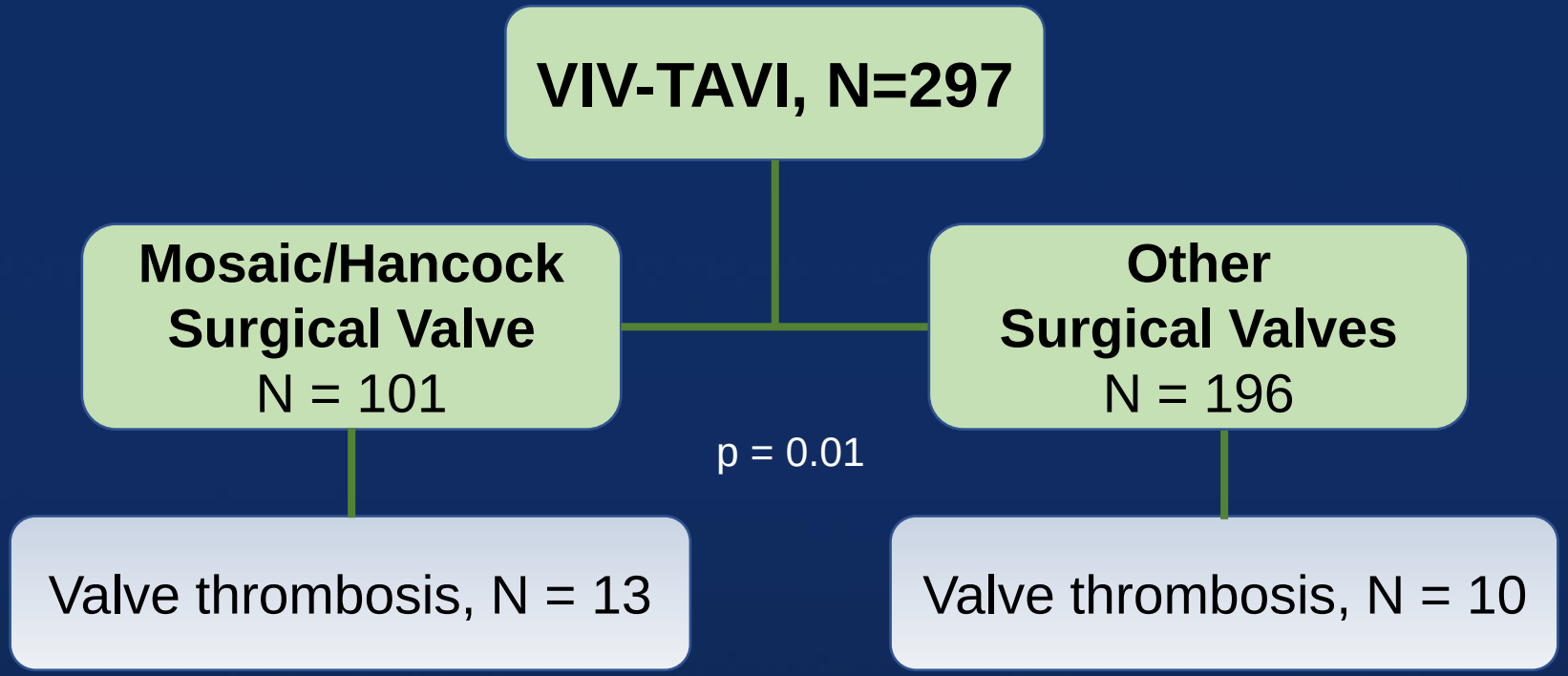



**Incidence of valve thrombosis on antiplatelets = 11.2%**

*Danny Dvir, MD. TVT 2017*

# Thrombosis after aortic VinV

## Incidence of valve thrombosis



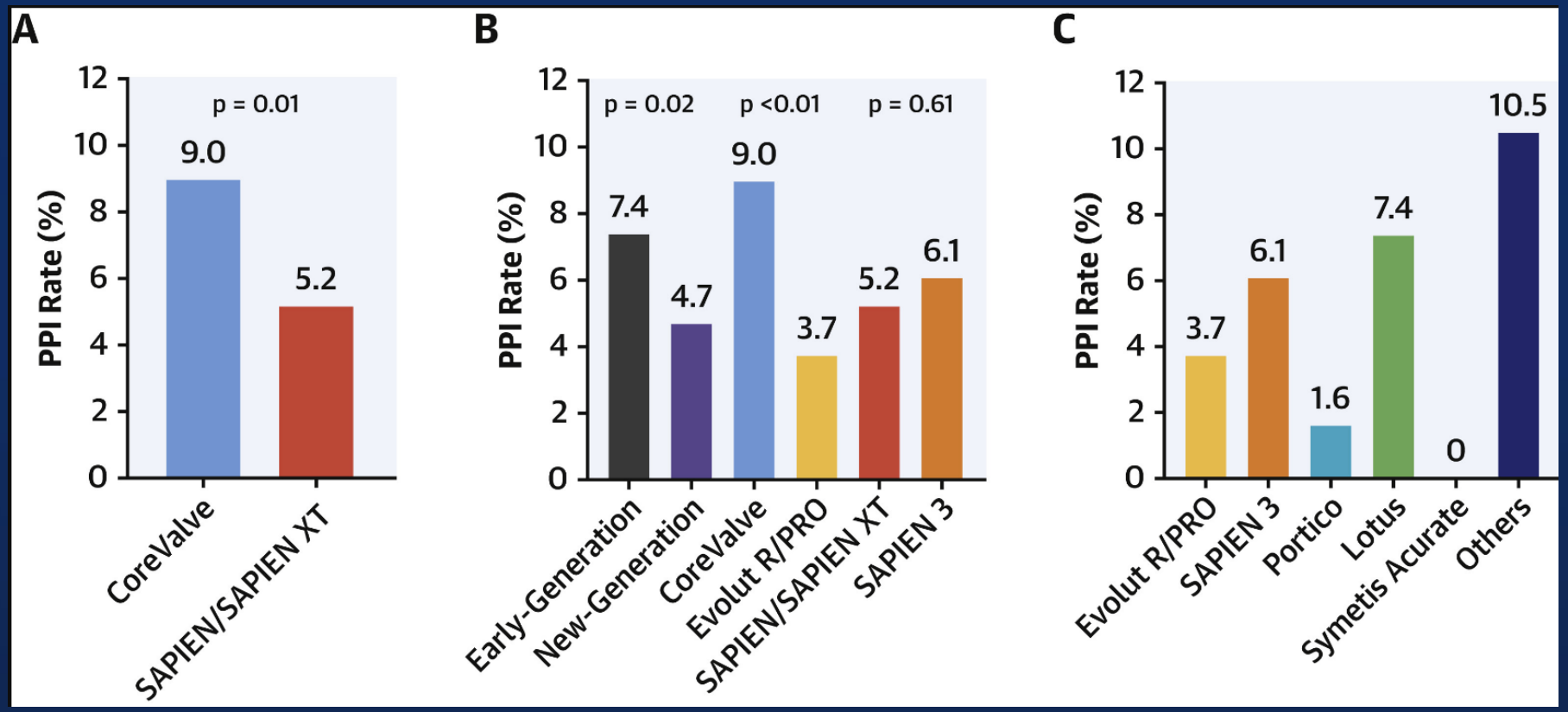

**Incidence of valve thrombosis after Mosaic/Hancock VIV = 12.9%**

**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

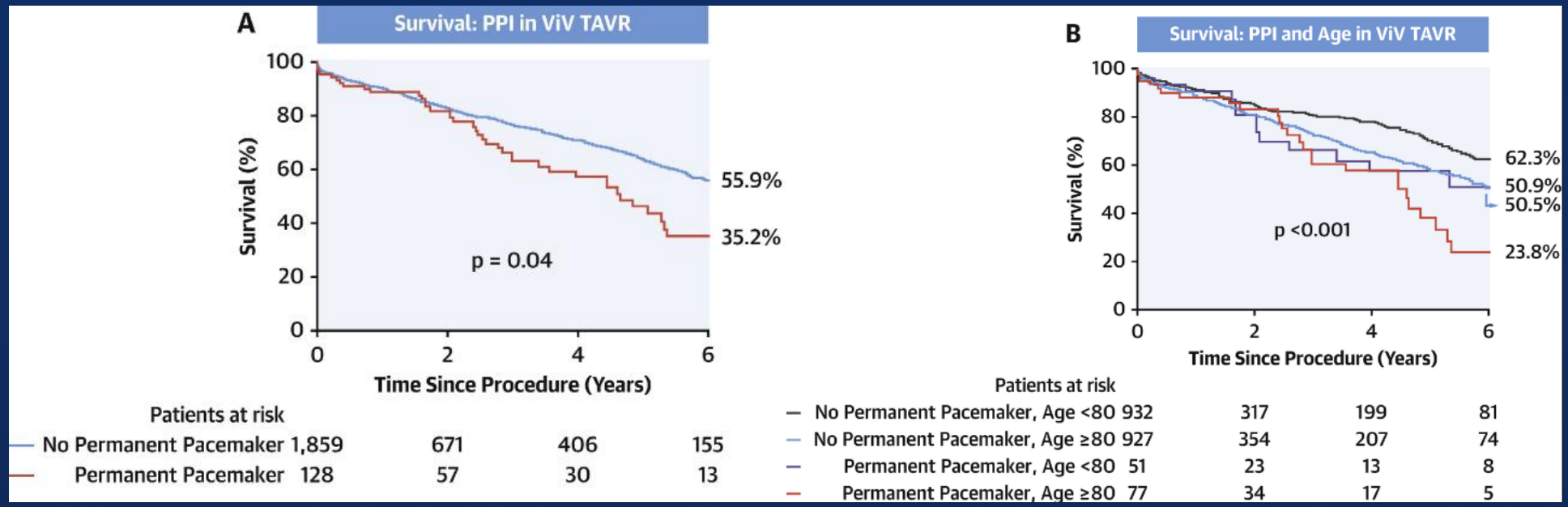
## PPI rate after ViV-TAVR for Early- and New-generation Devices




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

# Permanent pacemaker implantation after Valve-in-valve

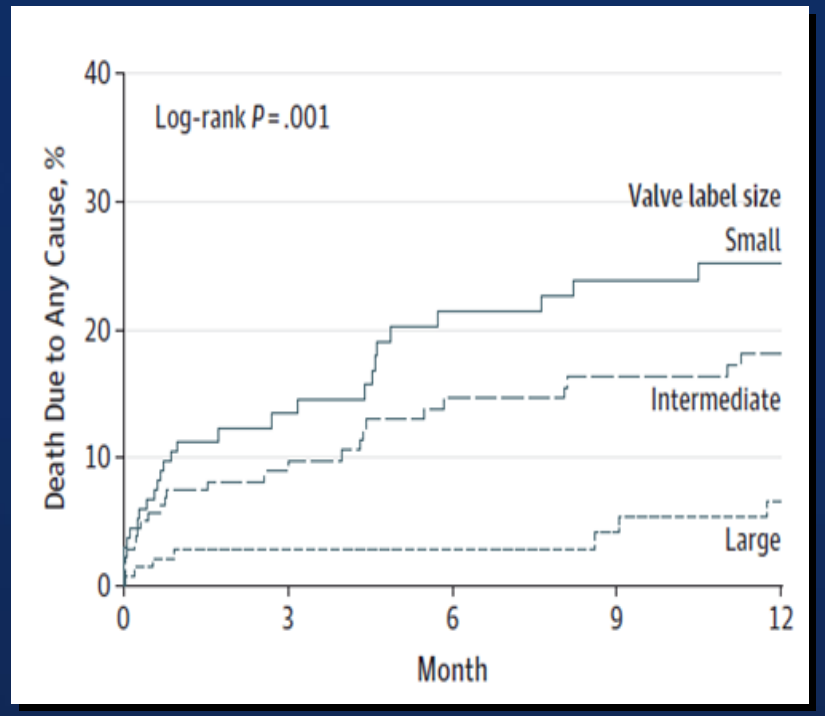
## Survival curve After ViV-TAVR by PPI and Age




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)

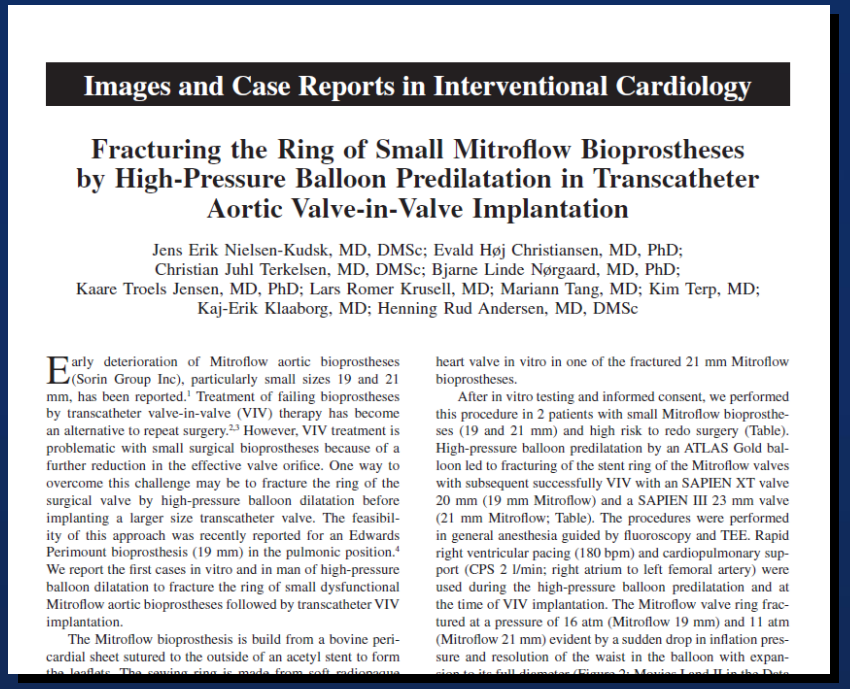
Dvir D, et al. JAMA 2014;312:162-170

# 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**

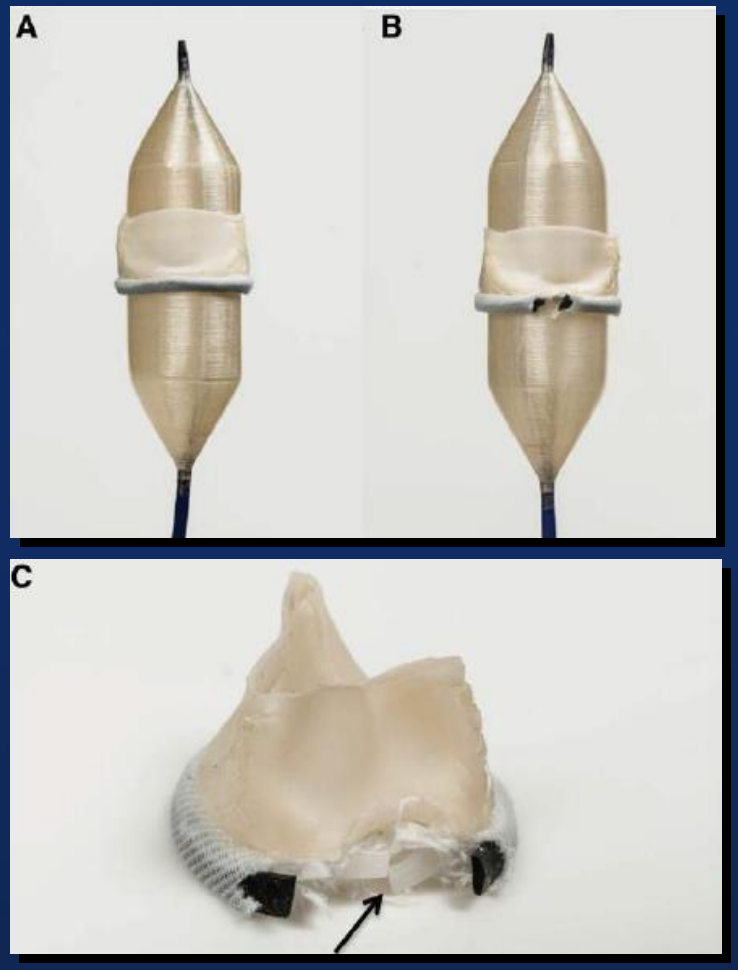
Jens Erik Nielsen-Kudsk, MD, DMSc; Evald Høj Christiansen, MD, PhD; Christian Juhl Terkelsen, MD, DMSc; Bjarne Linde Nørgaard, MD, PhD; Kaare Troels Jensen, MD, PhD; Lars Romer Krusell, MD; Mariann Tang, MD; Kim Terp, MD; Kaj-Erik Klaaborg, MD; Henning Rud Andersen, MD, DMSc

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 the leaflets. The sewing ring is made from soft radiopaque

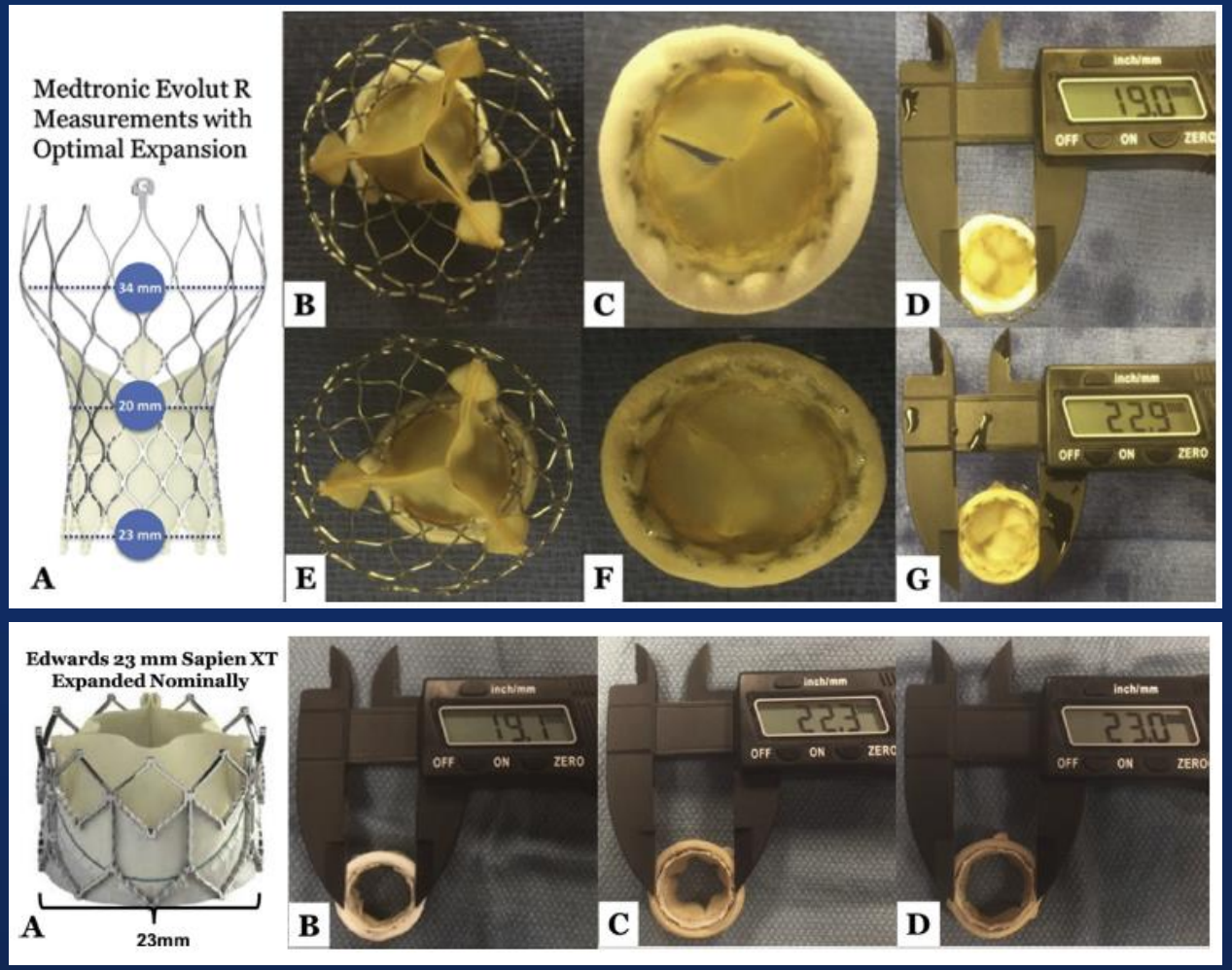
heart valve in vitro in one of the fractured 21 mm Mitroflow bioprostheses.

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



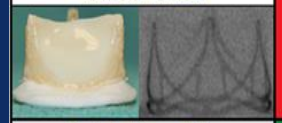
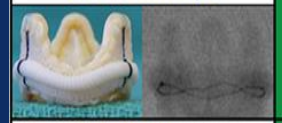
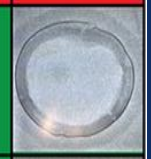
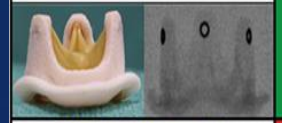
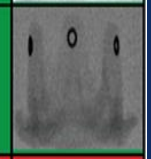
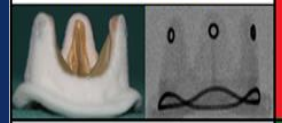
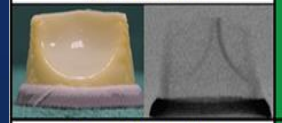
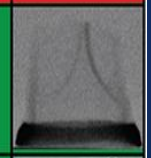
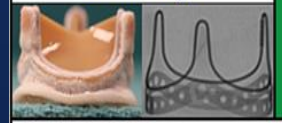

Allen KB, et al. Ann Thorac Surg 2017

# Valves that can and cannot be fractured

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

Trifecta (St. Jude)

Hancock II (MDT)

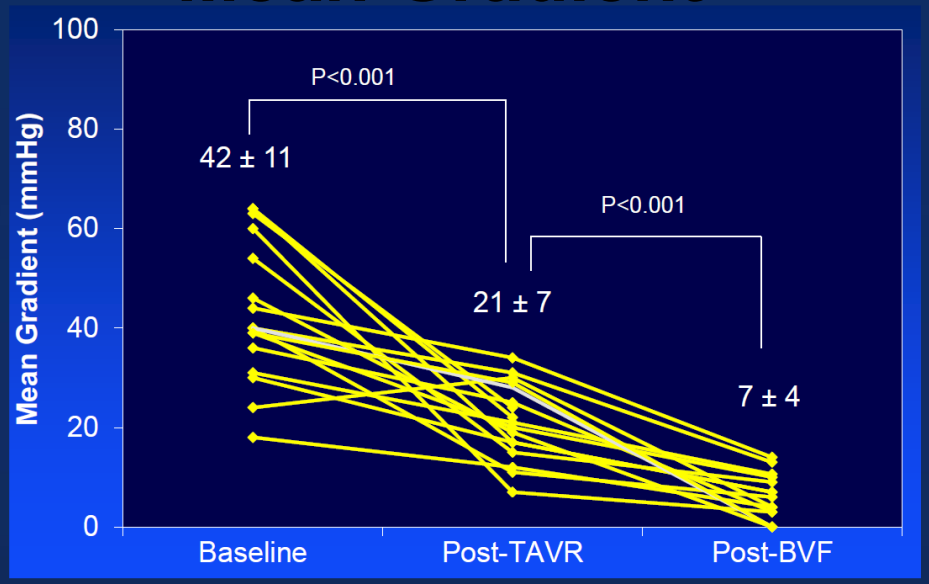
| Manufacturer/ Brand | Valve Size | Bard TRU Balloon Fracture/Pressure | Bard Atlas Gold Balloon Fracture/Pressure | Appearance After Fracture |
|---|---|---|---|---|
| St. Jude Trifecta  | 19 mm<br>21 mm | NO<br>NO | NO<br>NO | |
| St. Jude Biocor Epic  | 21 mm | YES / 8 ATM | YES / 8 ATM |  |
| Medtronic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

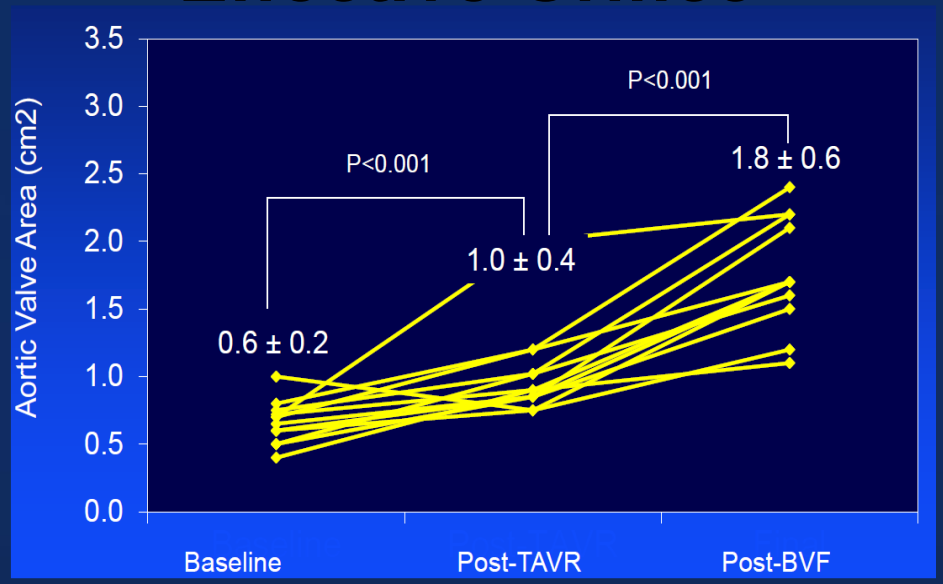
Allen KB et al. Ann Thorac Surg 2017

# Bioprosthetic Valve Fracture in VIV TAVR

## Mean Gradient



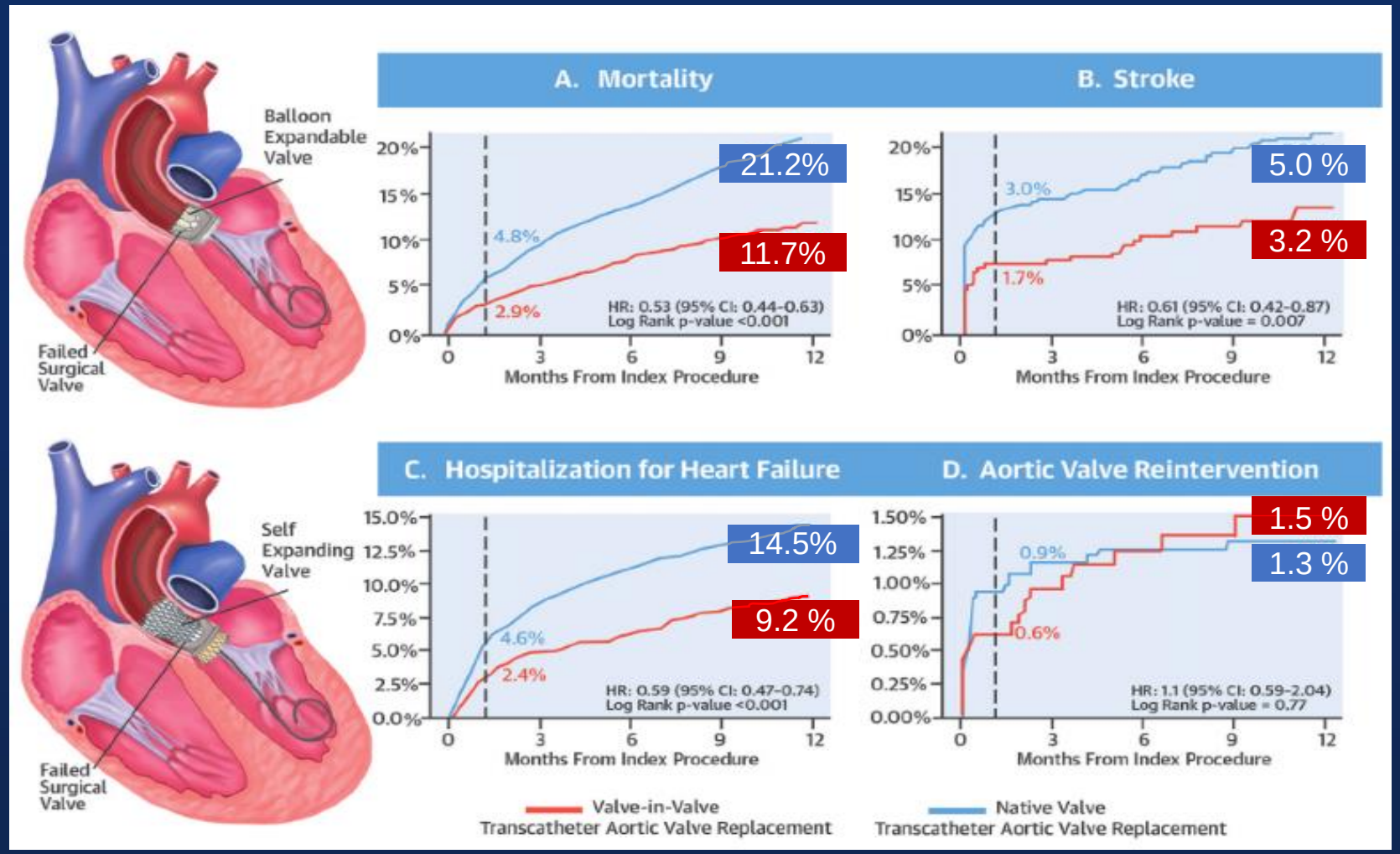

## Effective Orifice




**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)**

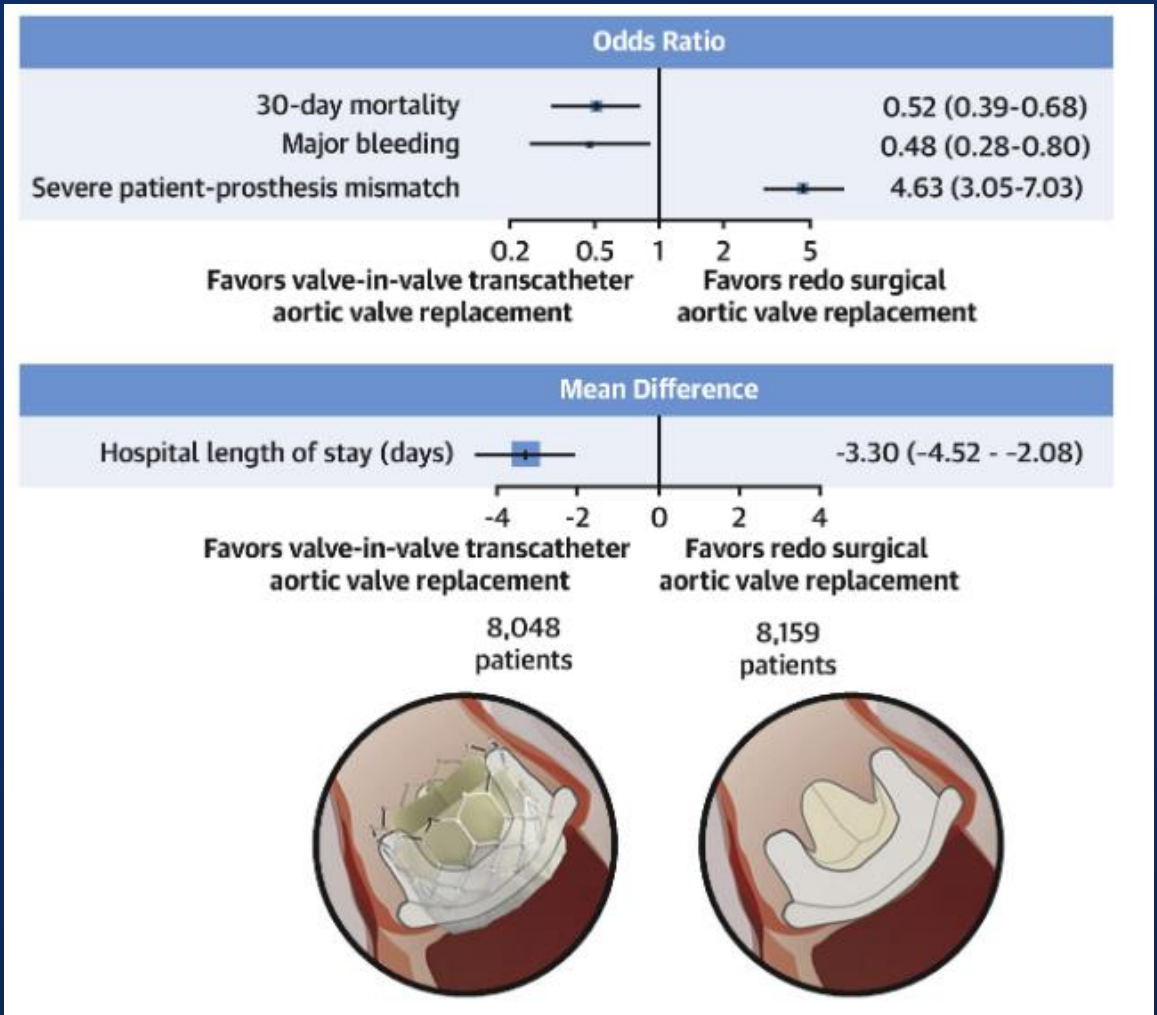
*David J. Cohen, MD. TVT 2017*
*Chhatriwalla A, et al. Circ Intv 2017*

# ViV TAVR Versus TAVR for Native Aortic stenosis



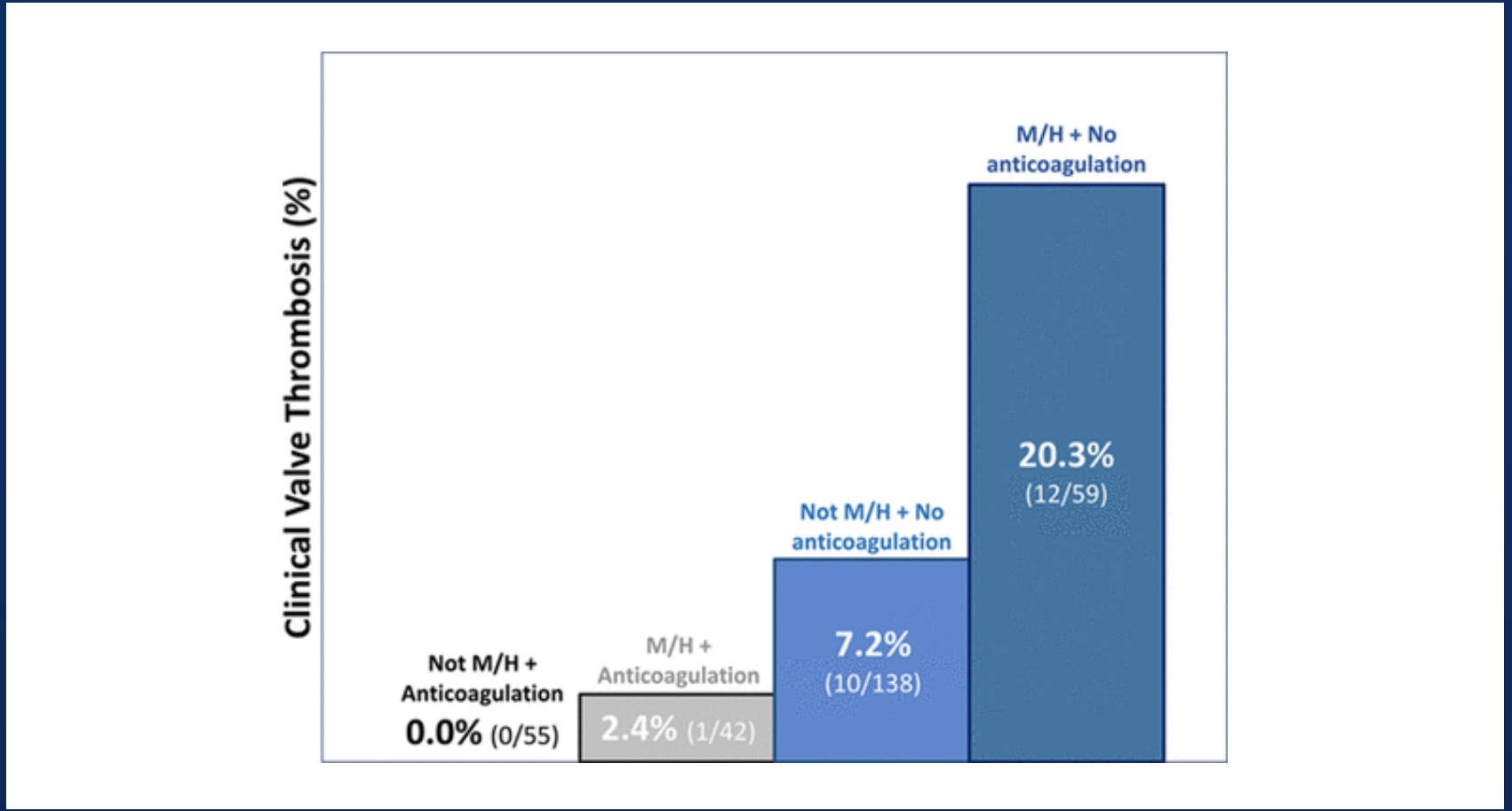

*Tuzcu, E.M. et al. JACC 2018*

# ViV TAVR Versus redo-SAVR for Bioprosthetic aortic valve dysfunction




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

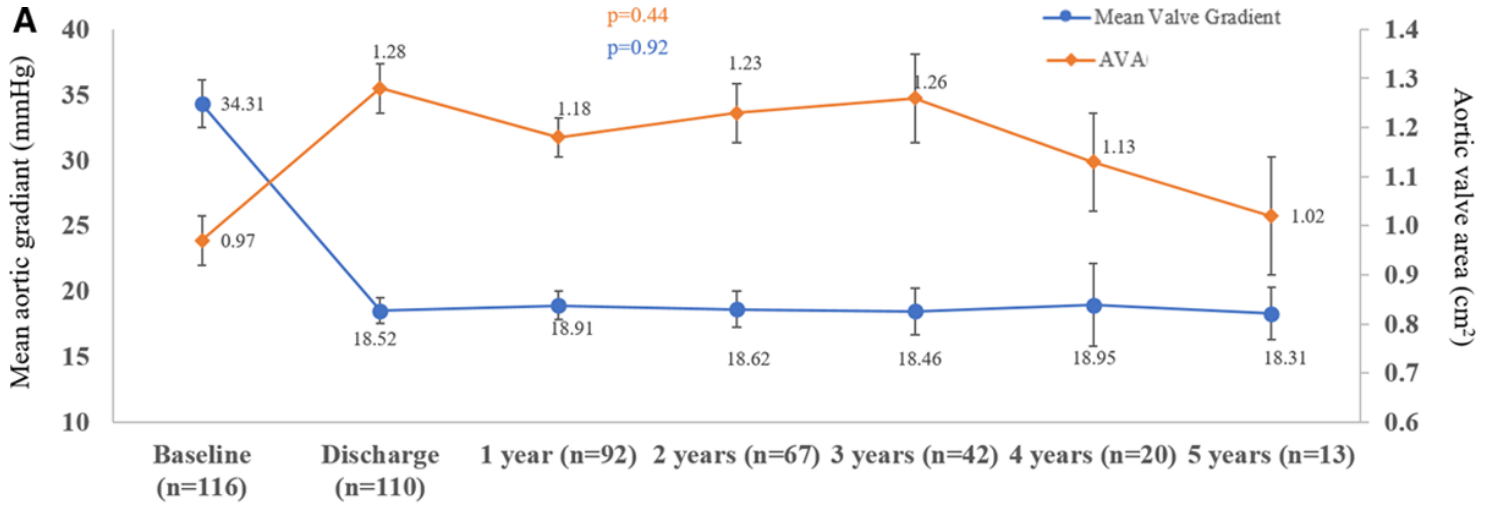
# Clinical Valve Thrombosis after Transcatheter Aortic ViV Implantation






*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

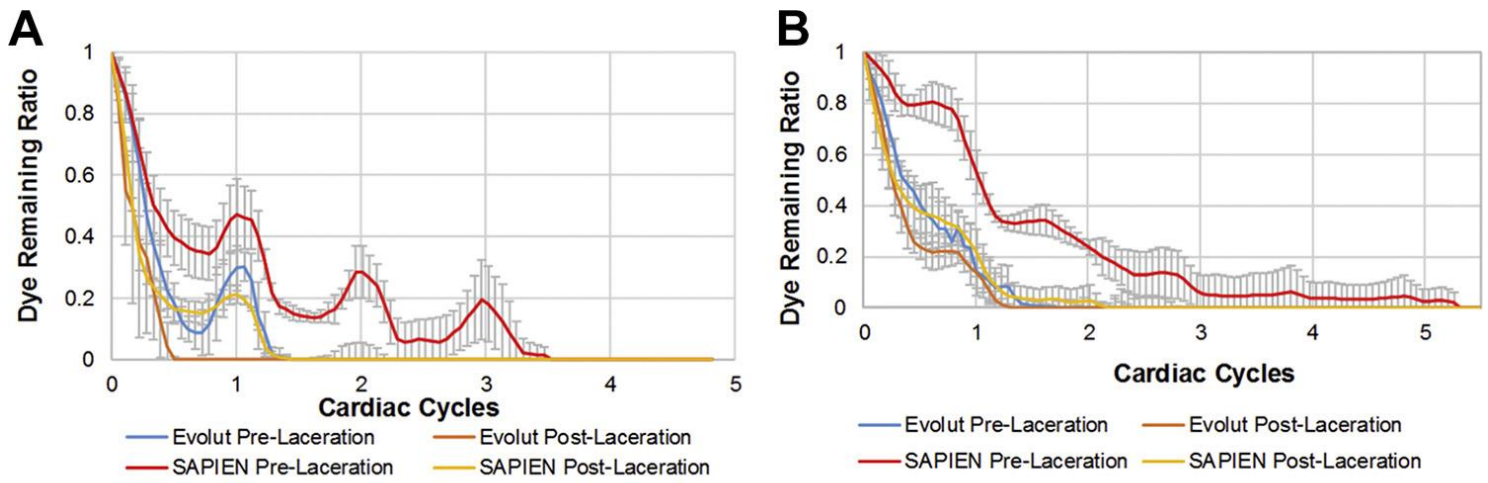
- **Among 66 SBAV, Mortality 3.0% at 30 days and 9.6% at 1 year.**
- **At 1 year, LVED was decreased versus baseline : 3.0 [2.6 to 3.6] cm vs. 3.7 [3.2 to 4.4] cm (p < 0.001)**
- **Coronary occlusion (9.1%) resulted in myocardial infarction (3.0%).**
- **Predictors of coronary occlusion**
  **Subcoronary 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.



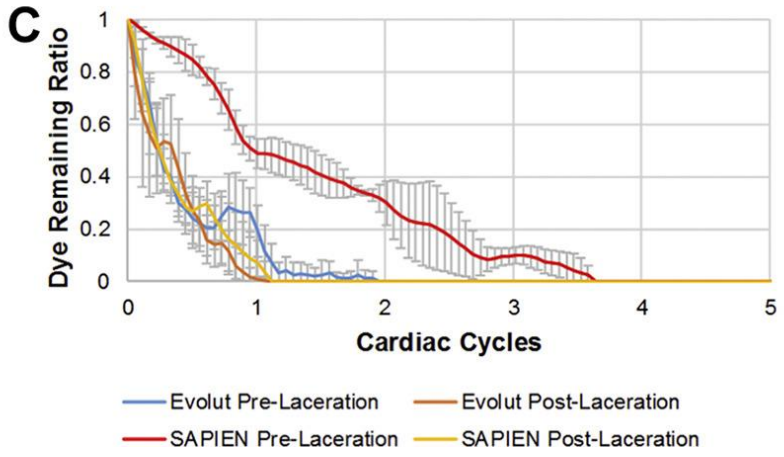
*Miller M, et al. JACC Intv 2019*

# Impact of Leaflet Laceration on Transcatheter Aortic ViV Washout





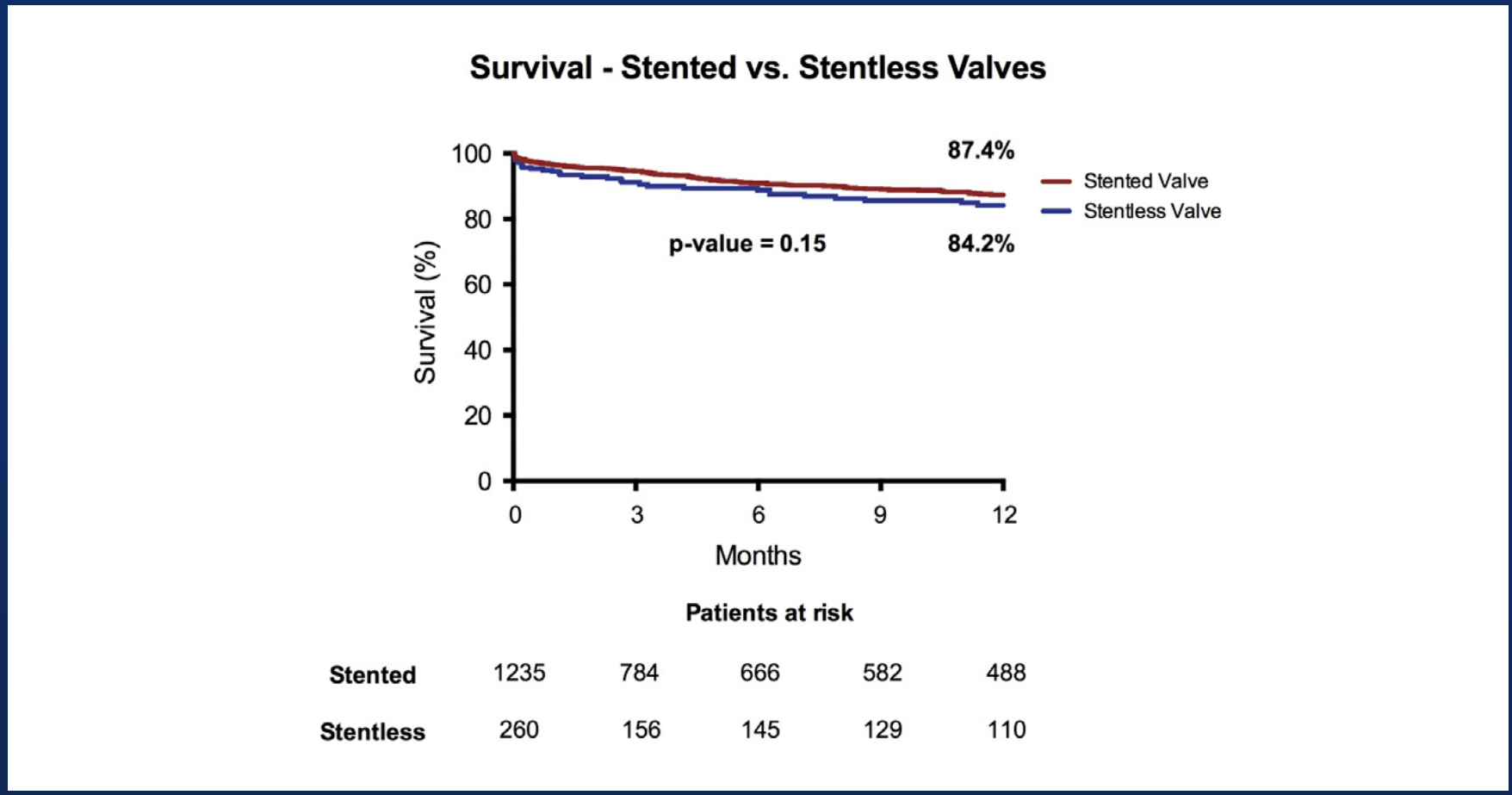







*Hoda Hatoum et al, JACC intv 2019*

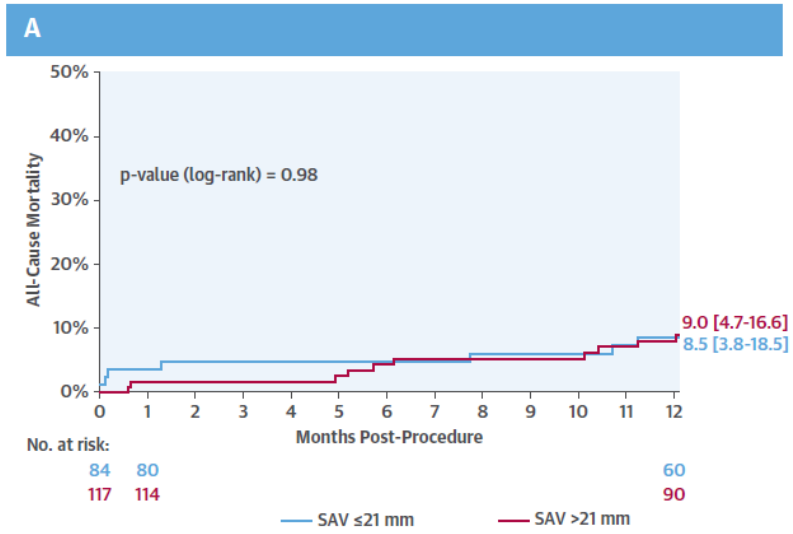
# ViV-TAVR
# Stentless vs stented Valves

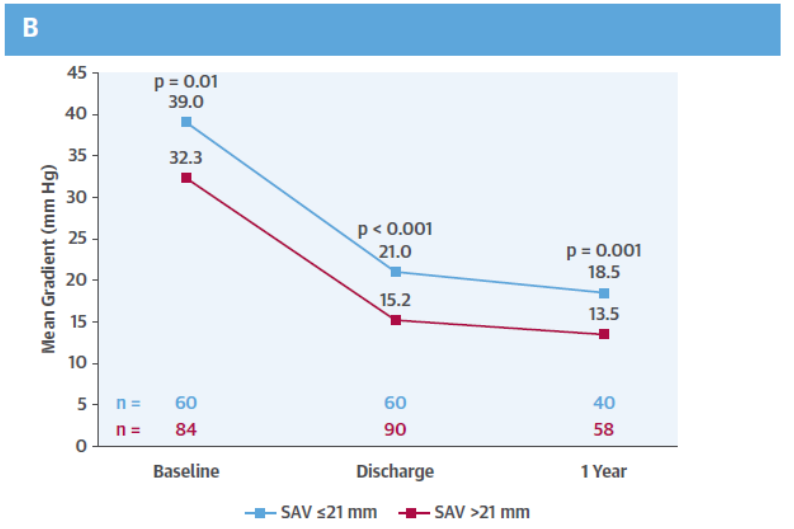





*Duncan et al., JACC intv 2019*

# Clinical and Echocardiographic Outcomes According to Surgical Valve Size

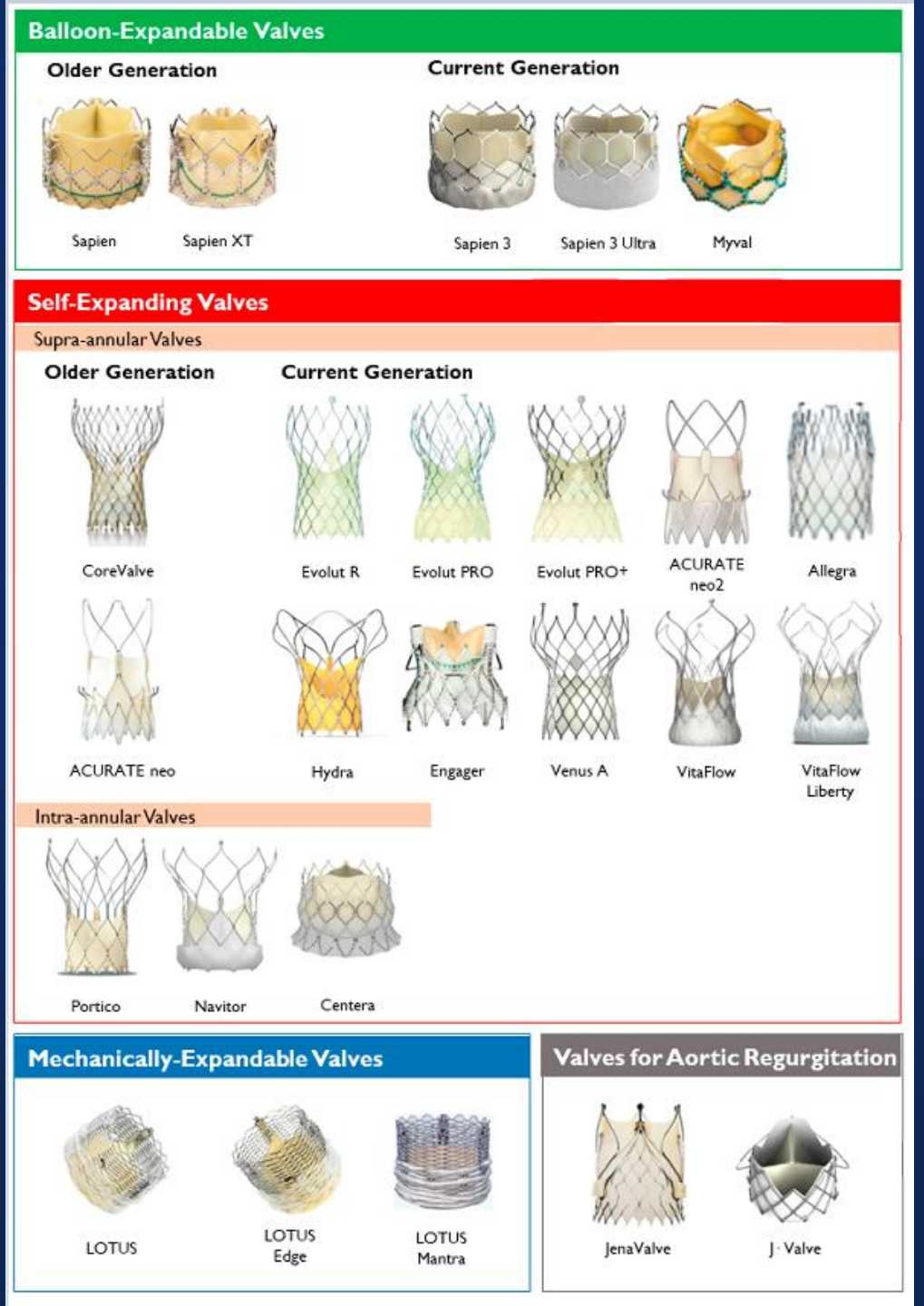



*Tchétché, D. et al., JACC Intv 2019*

# New TAVR Devices

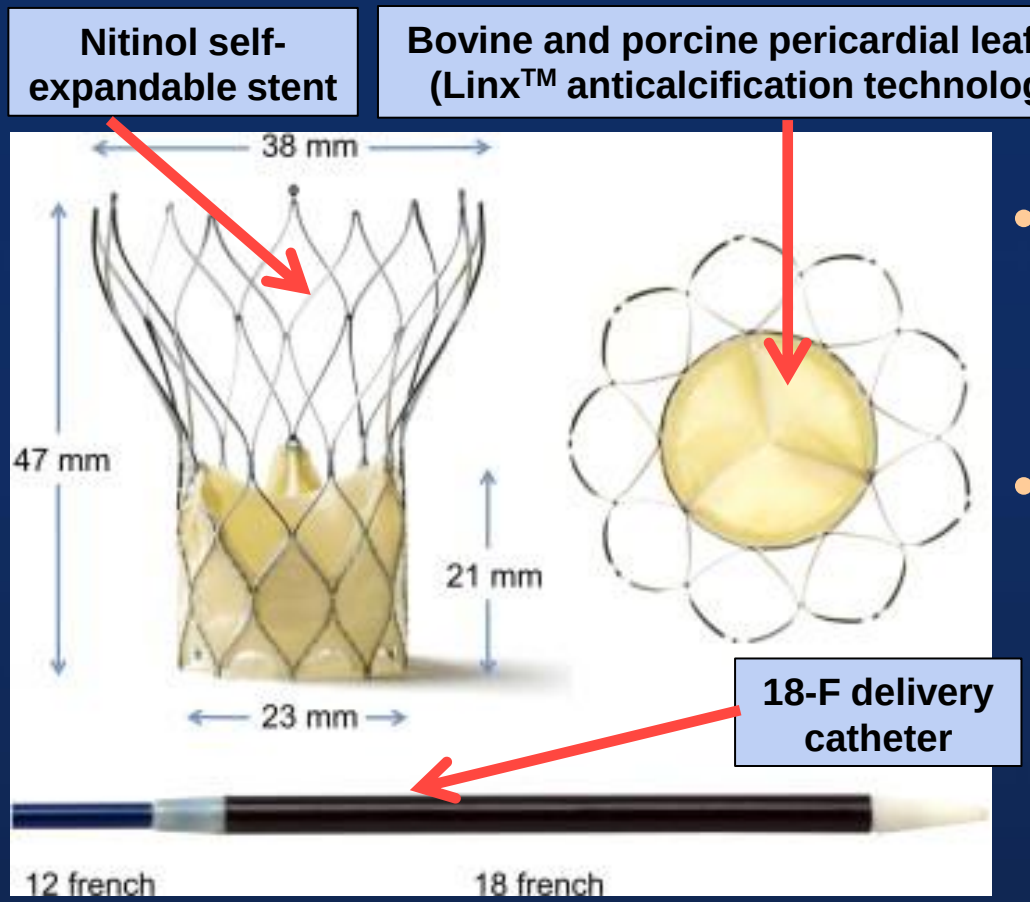
# Older & Current




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

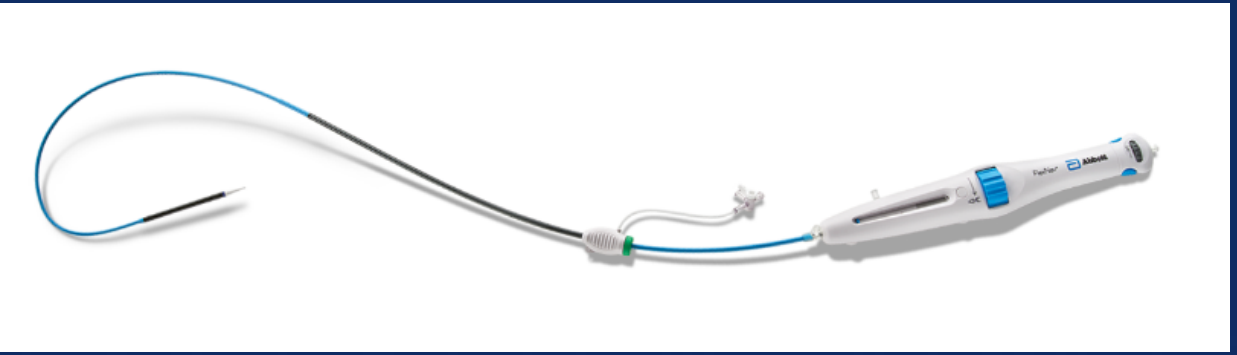
# TAVR with St. Jude Medical Portico Valve: First-in-Human Experience

**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 ($P < 0.001$)

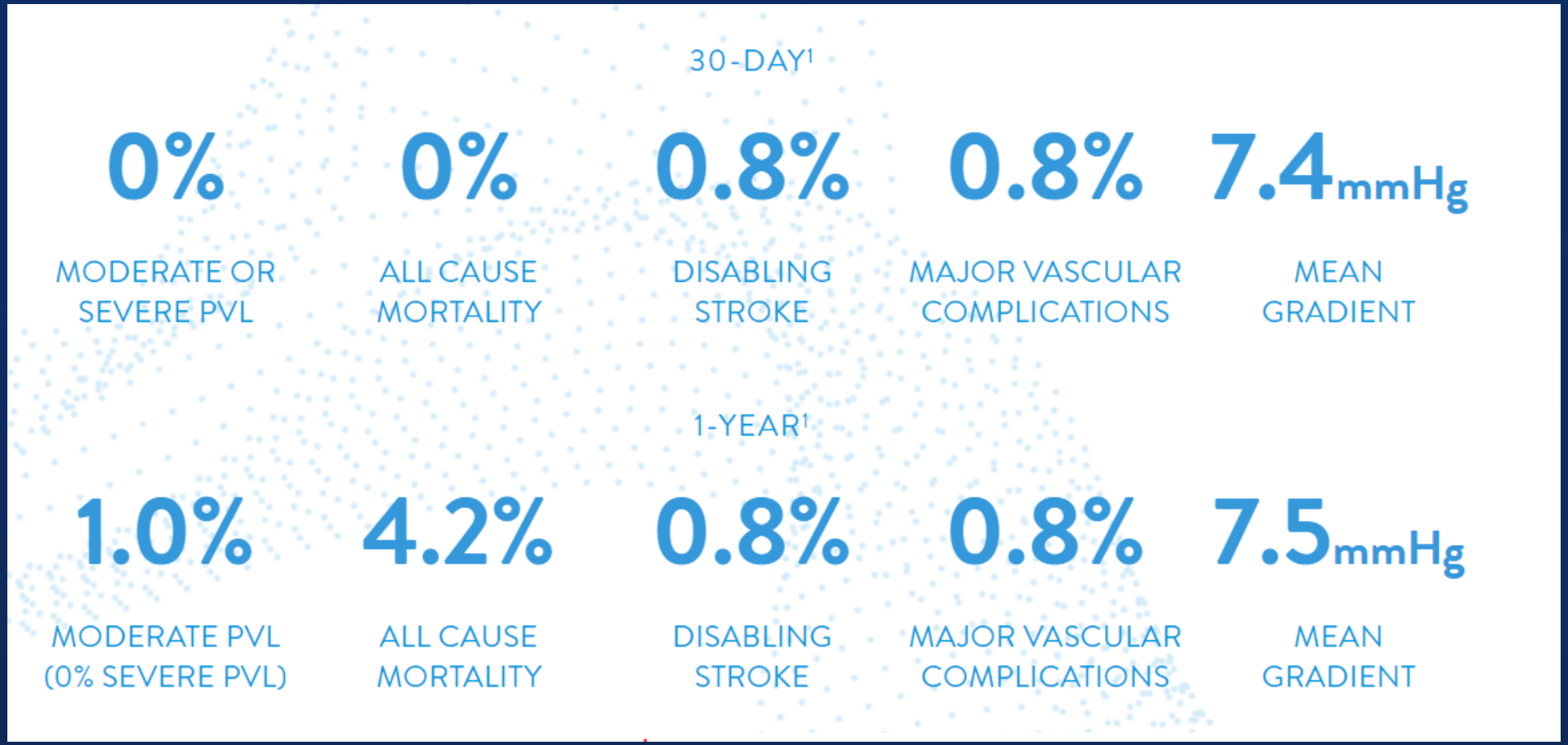
J Am Coll Cardiol. 2012 Aug 14;60(7):581-6. Epub 2012 May 30

# Navitor™



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

# Navitor™



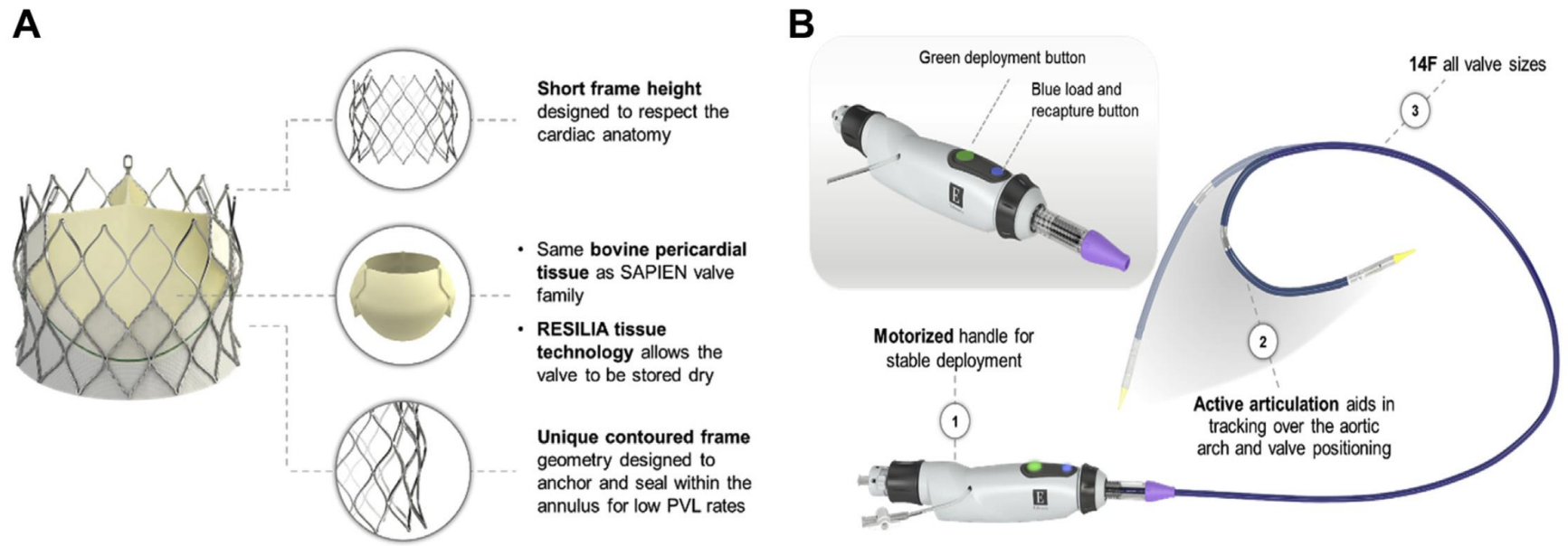


1.Smith, D. One-year clinical trial results with a next-generation aortic transcatheter heart valve. Presented at: EuroPCR conference; May 17-20, 2022.
2.Forrest JK, Mangi AA, Popma JJ, et al. Early outcomes with the Evolut PRO repositionable self-expanding transcatheter aortic valve with pericardial 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

**FIGURE 1** CENTERA Transcatheter Aortic Valve and Delivery System




**(A)** Structure of the CENTERA self-expanding transcatheter heart valve. **(B)** Characteristics of the CENTERA delivery system. PVL = paravalvular leak.

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.

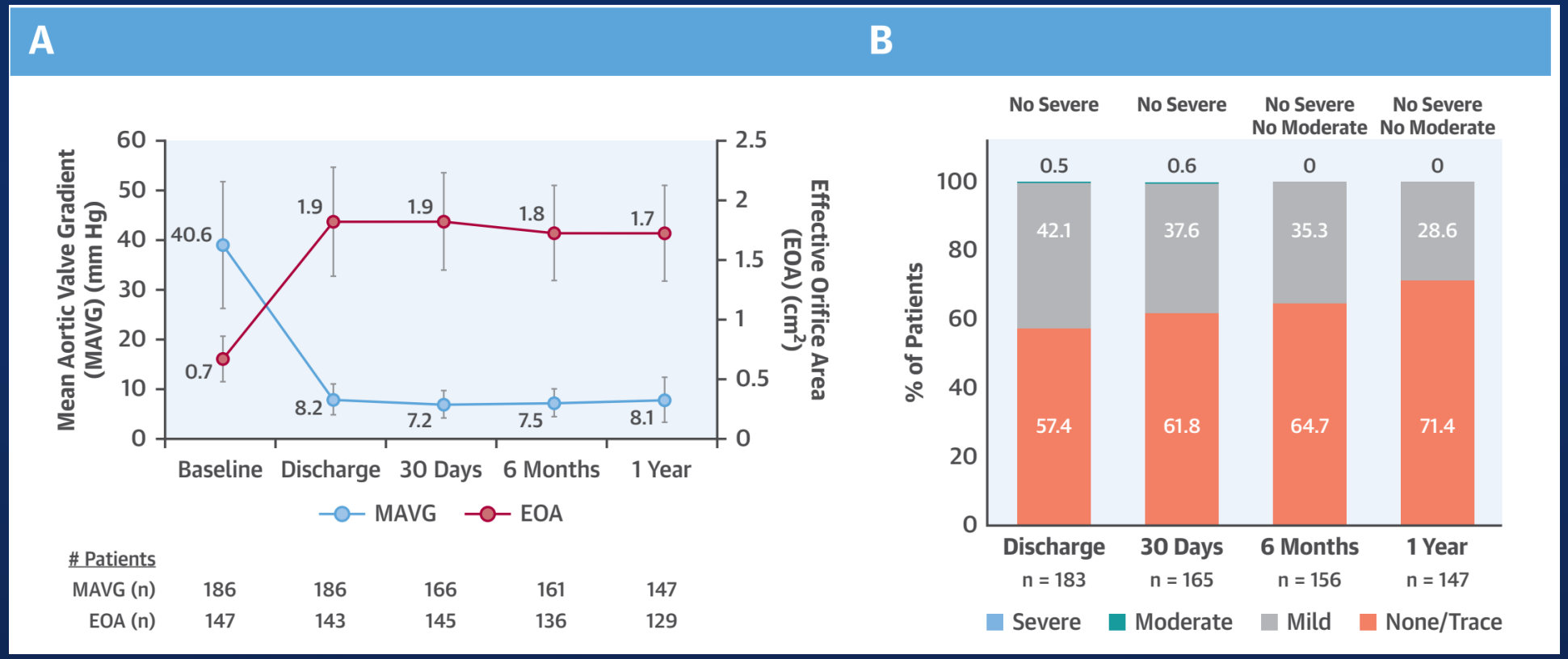
CEC = Clinical Events Committee; NA = not applicable; PPMI = permanent pacemaker implantation.



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

# CENTERA

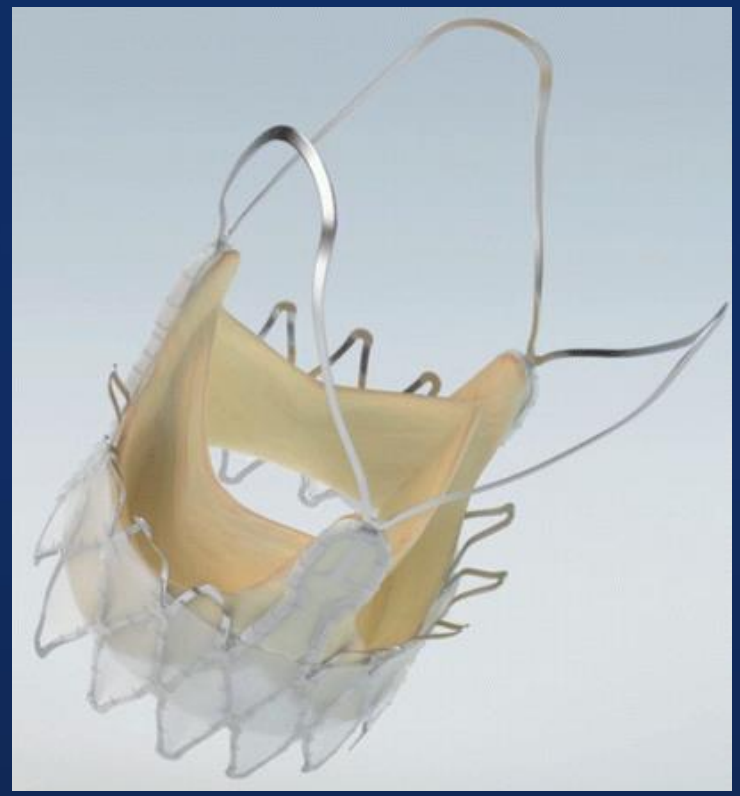
## 1 year outcomes from CENTER-EU trial






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

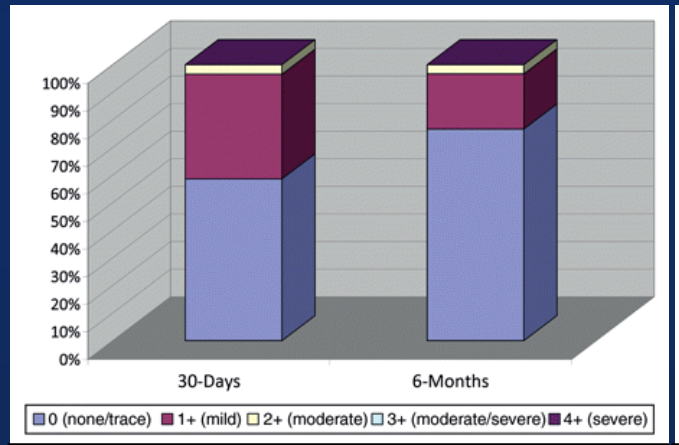
# Symetis Acurate TA™ Aortic Bioprosthesis



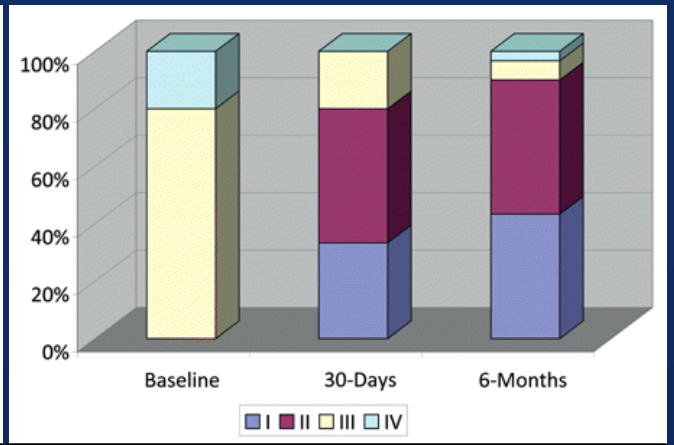
- Porcine pericardium
- Self-expanding nitinol stent
- Stent covered inside and out with double porcine pericardium skirt

# 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

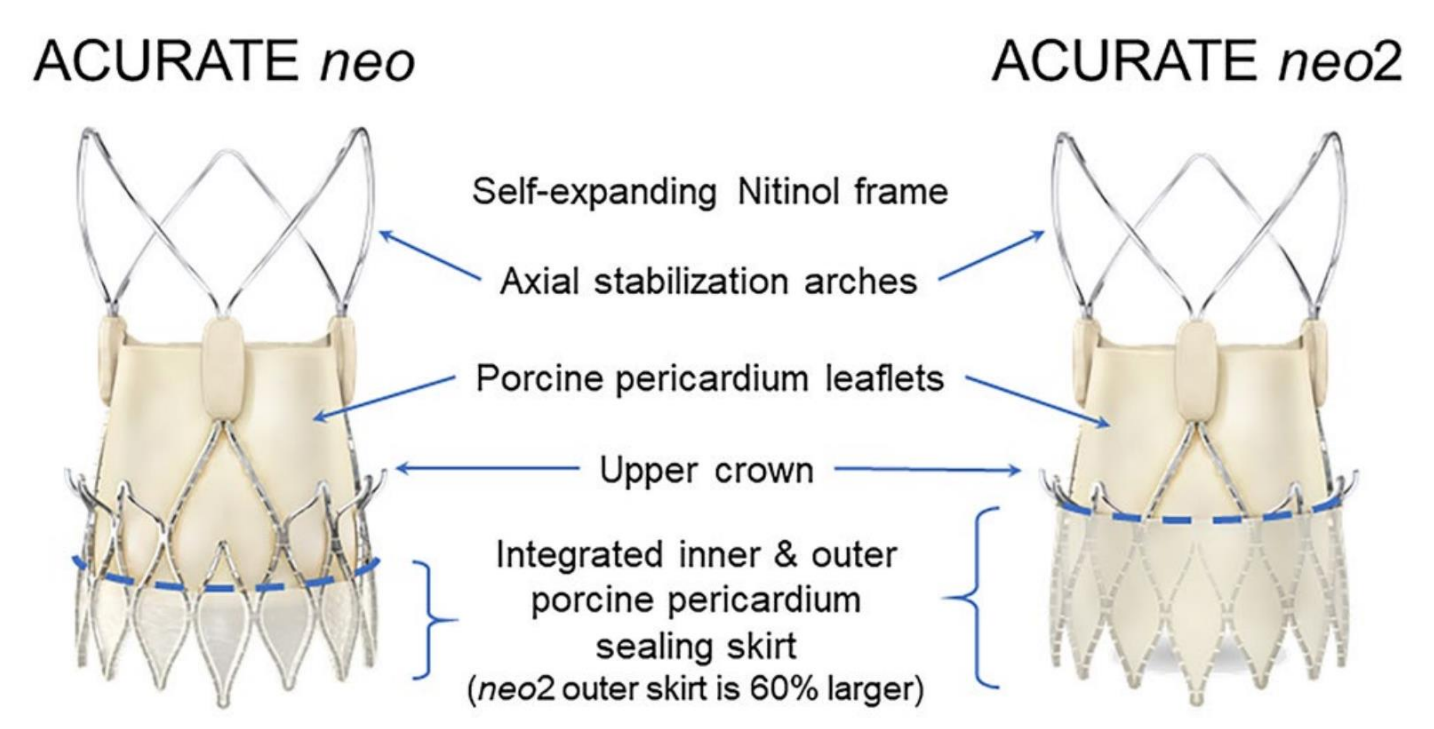
- **Trans Apical**
  - Pilot (n=50) 30days results (TCT 2011)
  - FIM (n=40) 1Y results (AHA 2011)
  - Pivotal (n=150) enrollment start, 2011(4th quarter)
  - SAVI post-market registry (n=250) with commercial implants

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

# ACURATE neo2

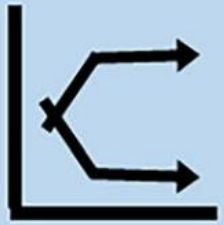
## ACURATE *neo2* demonstrates sustained safety and performance for TAVI

### 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

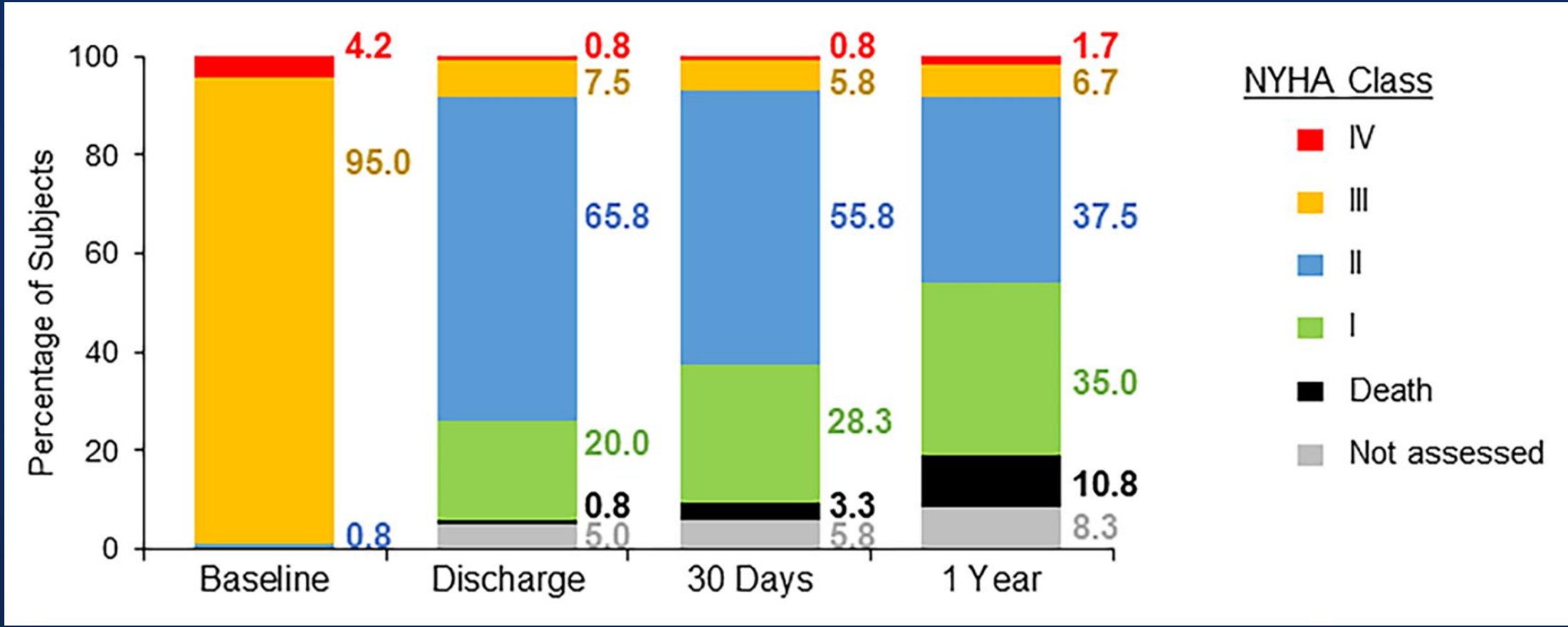




Clinical Research in Cardiology (2021) 110:1912–1920

# 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

# ACURATE neo2

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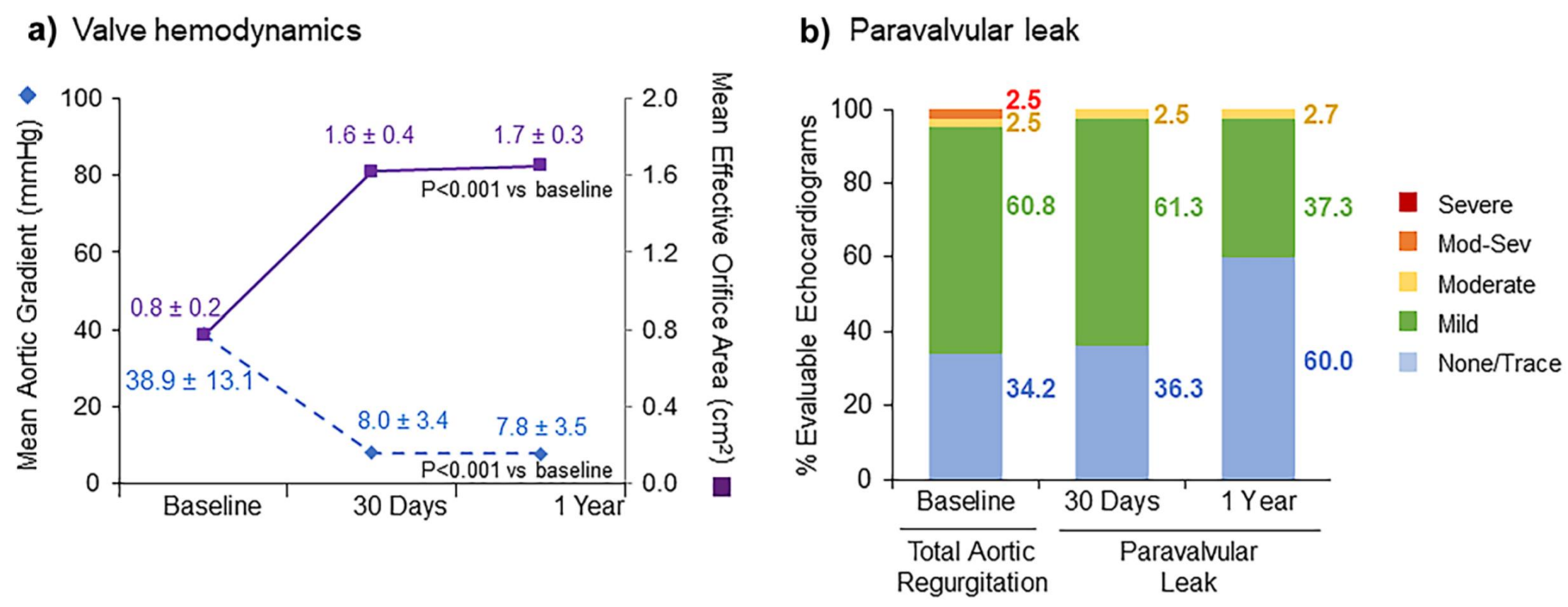





Clinical Research in Cardiology (2021) 110:1912–1920

# ALLEGRA

**Durability**

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

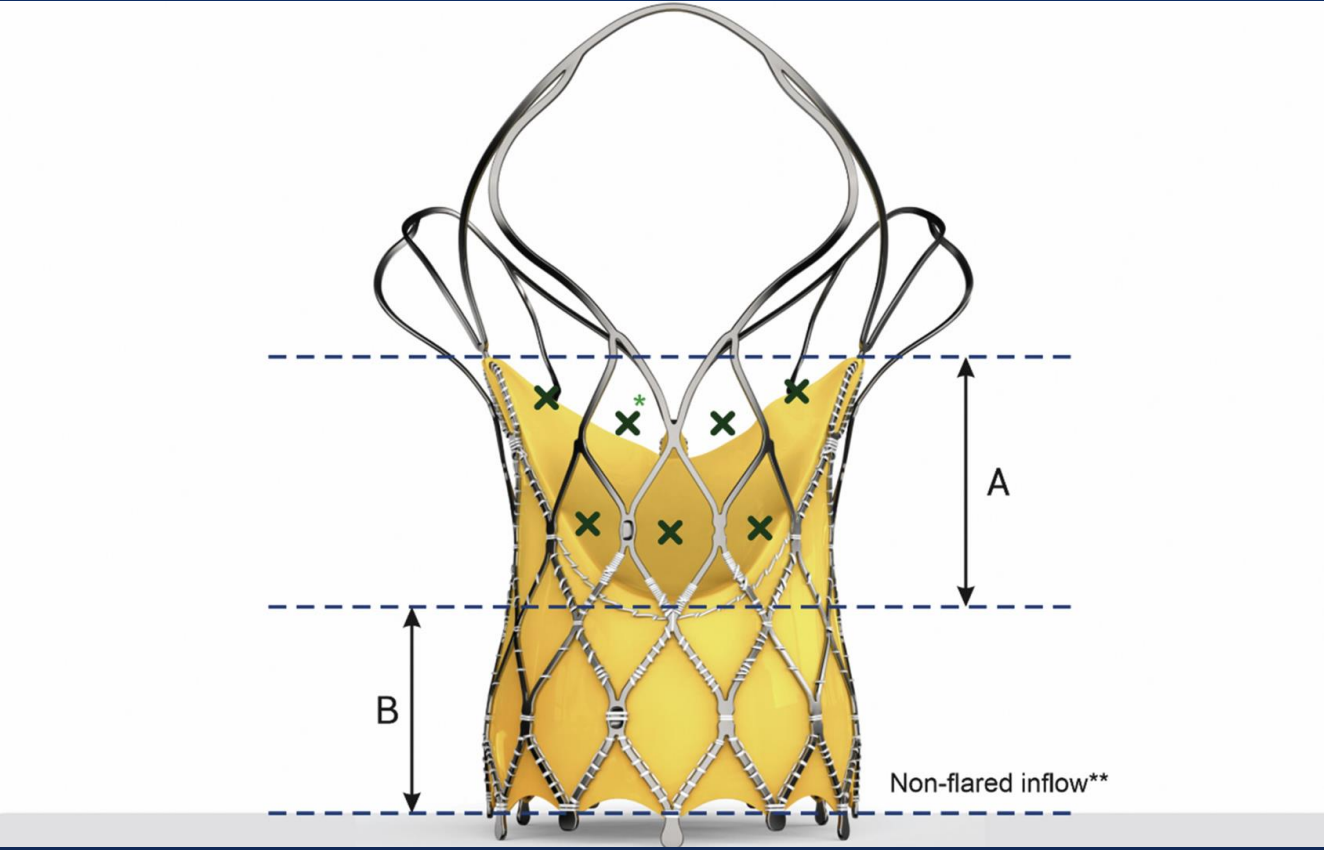
**Control**

- 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

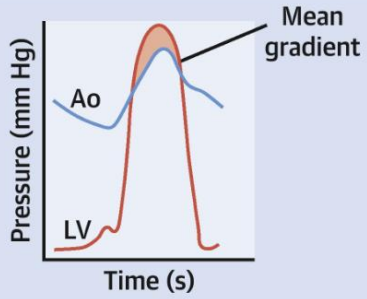


Aidietis, A.et al. J Am Coll Cardiol Intv. 200;15(1):93-104.

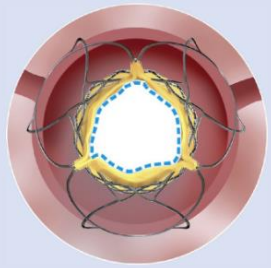
# Hydra

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

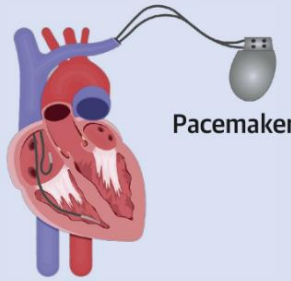
**Hydra Transcatheter Heart Valve Offered Favorable Efficacy as Well as Low Complication Rates: Hydra CE Study**




Mean aortic valve gradient at 30 days: 8.1 mm Hg

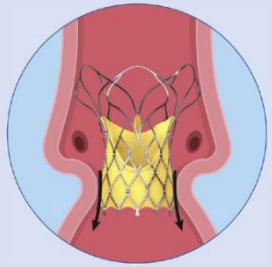


Mean effective orifice area at 30 days: 1.9 $cm^2$




New permanent pacemaker at 30 days: 11.7%

Hydra Transcatheter Heart Valve



≥ 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

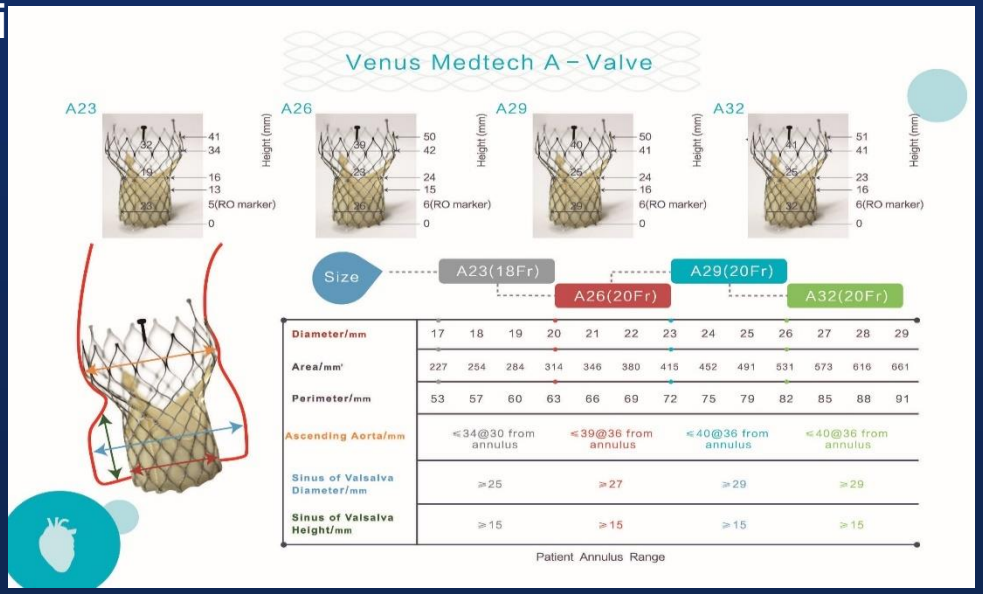
Medtronic Engager valve platform has NOT obtained CE Mark.
It is not approved in the EU or the US for commercialization.

**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



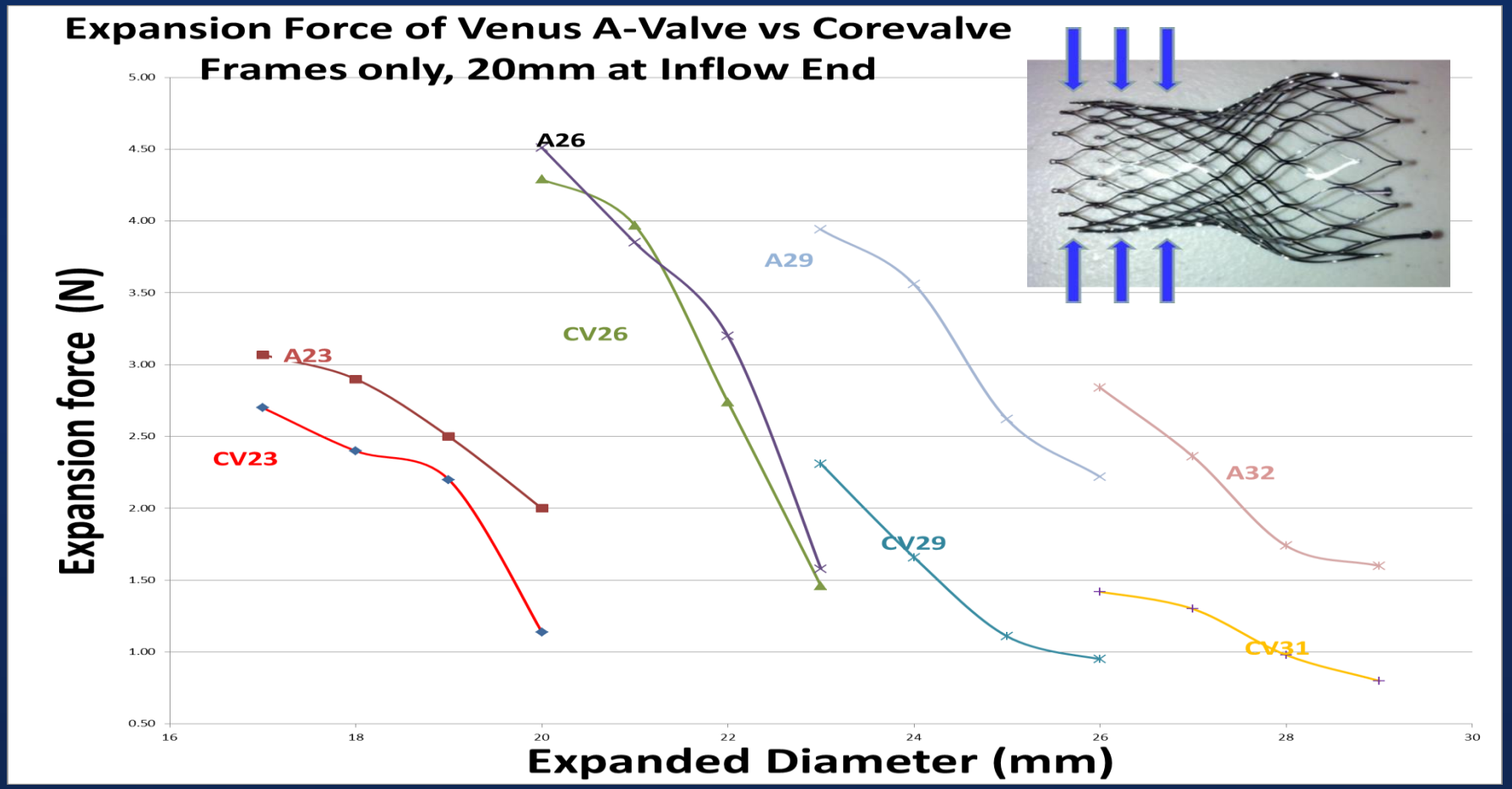
# Venus valve

**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

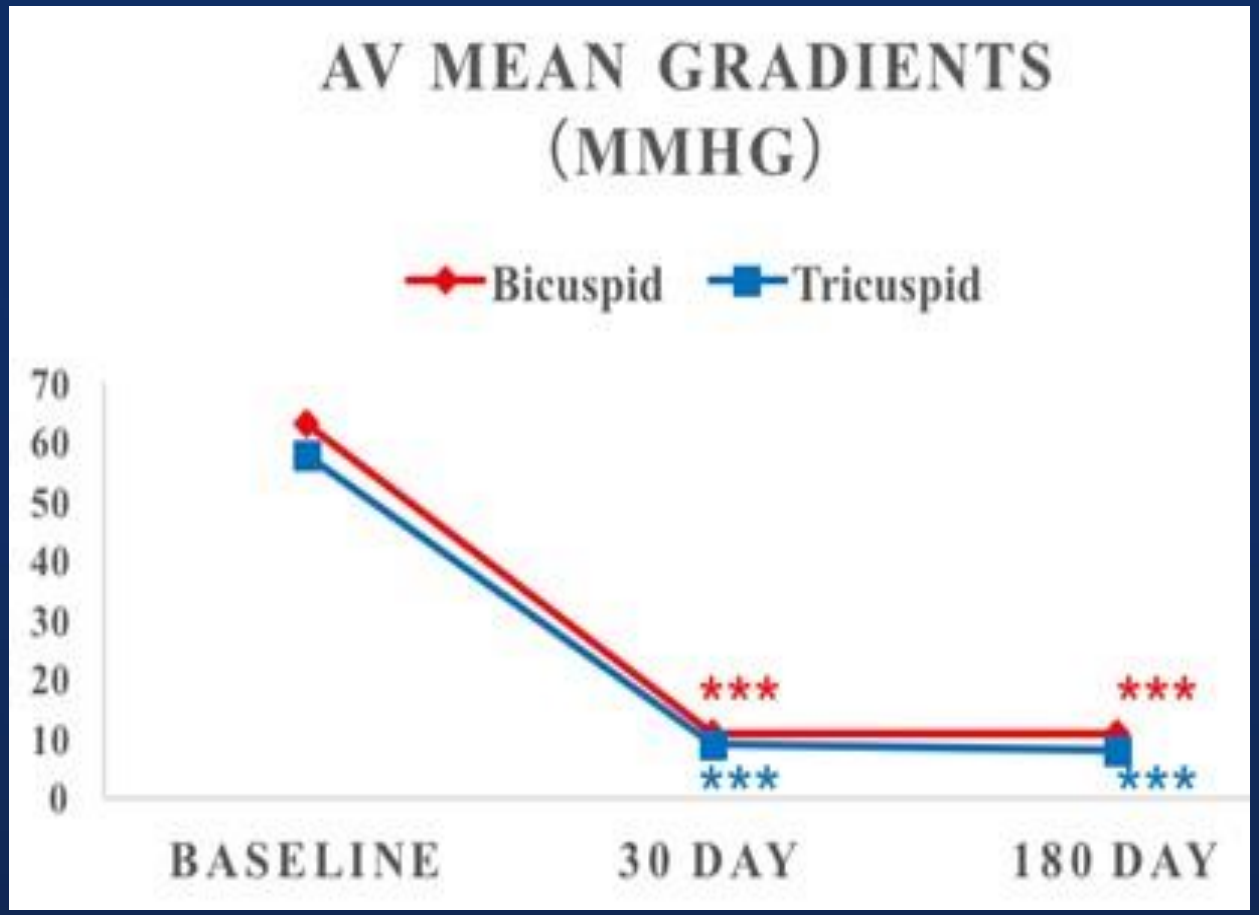
# Venus A-Valve
## Adverse Events

| | 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

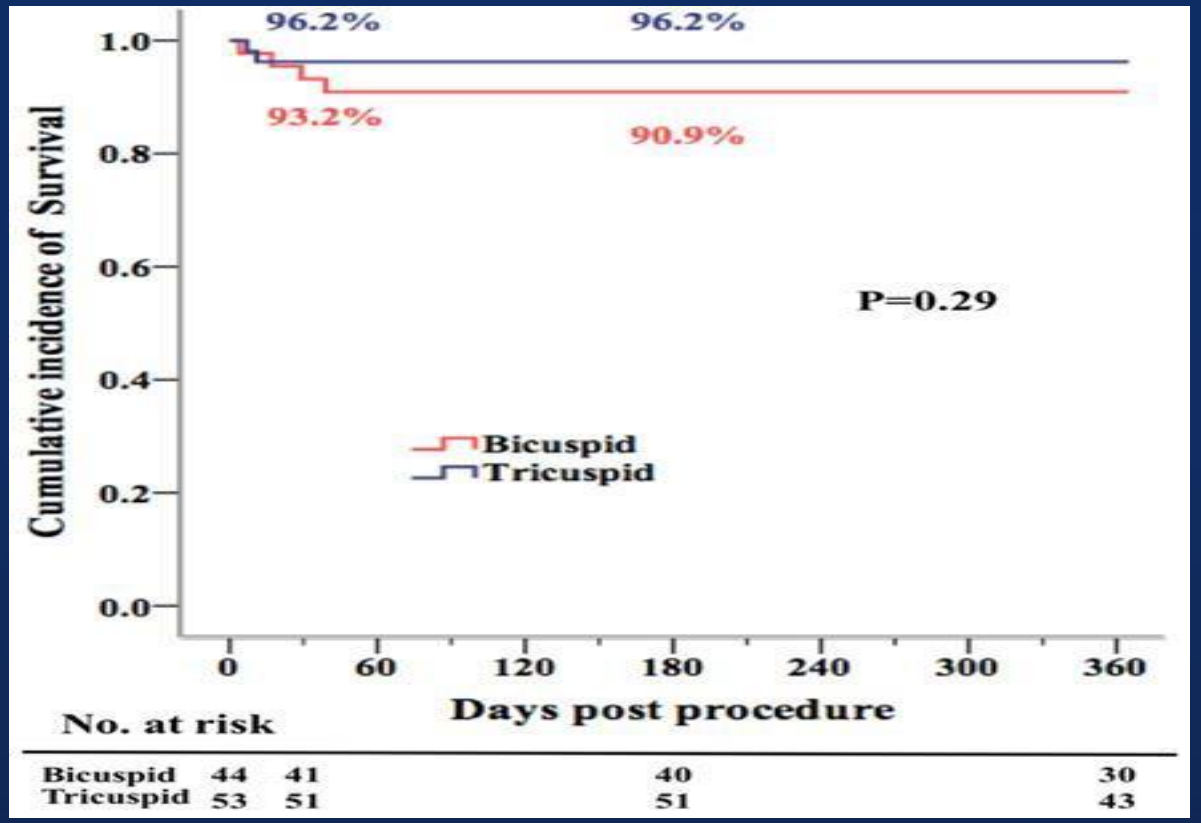
## Venus-A trial




Hasan Jilaihawi, TCT 2016

# Venus A-Valve in Bicuspid AV

## Venus-A trial

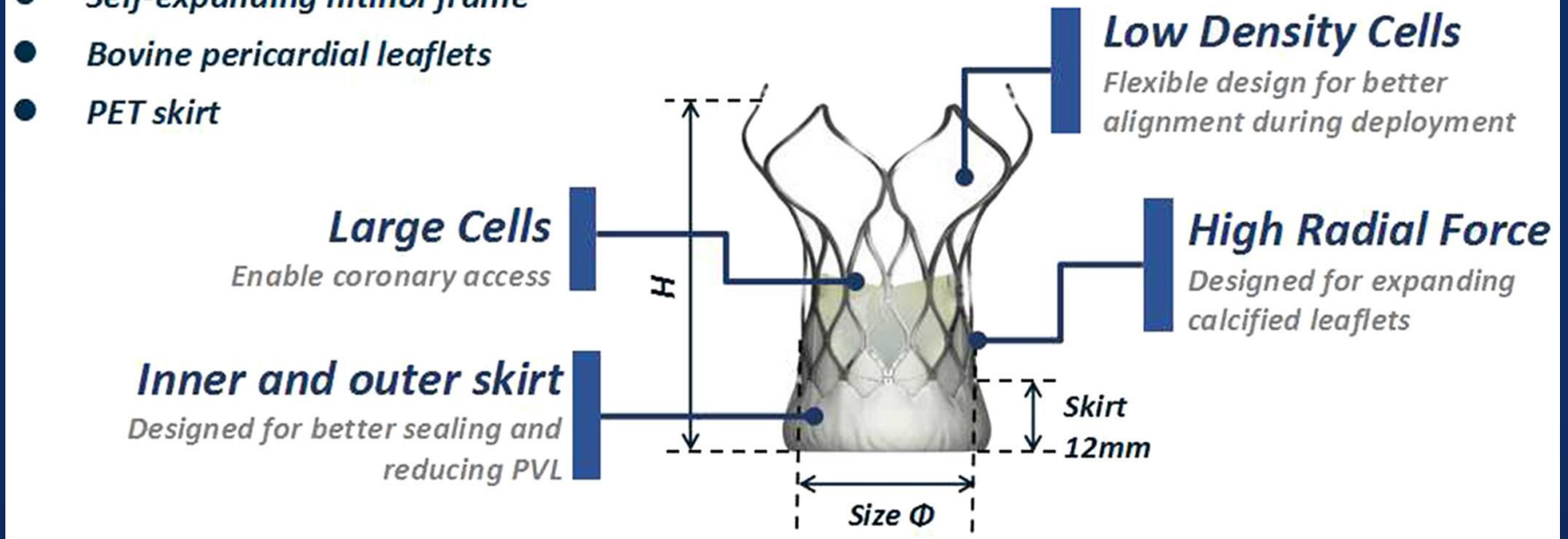



Hasan Jilaihawi, TCT 2016

# VitaFlow

## VitaFlow™ Aortic Valve

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



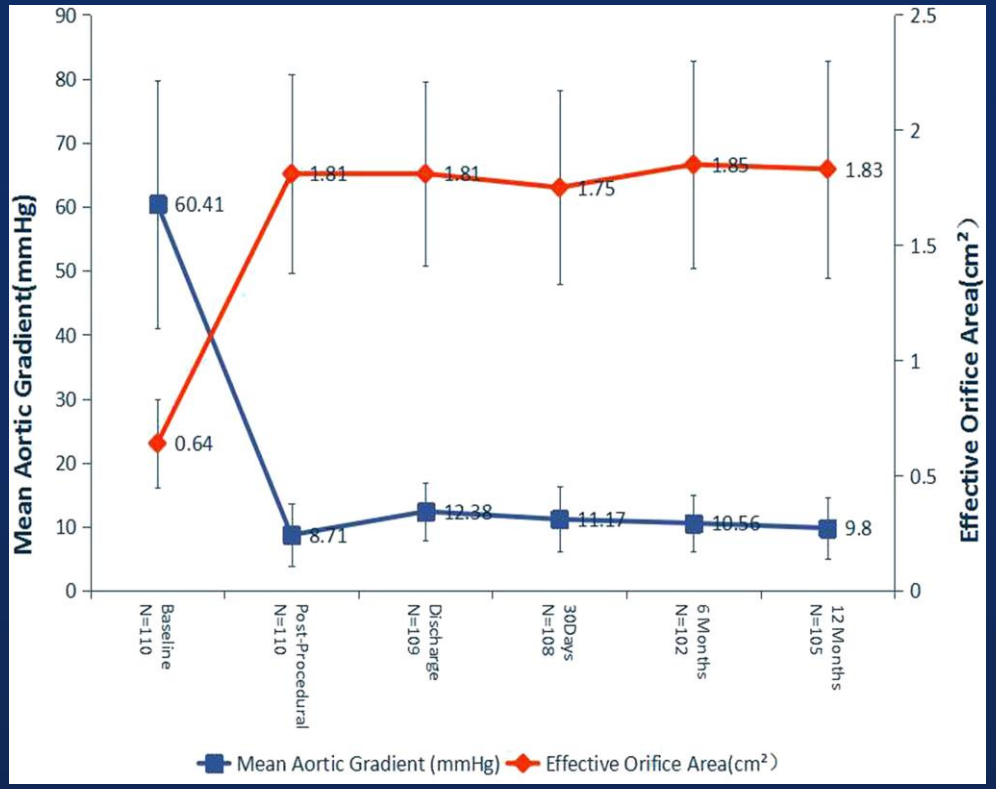

| Size Φ | 21mm | 24mm | 27mm | 30mm |
|---|---|---|---|---|
| Aortic Annulus Diameter | 17-20mm | 20-23mm | 23-26mm | 26-29mm |
| Height H | 50mm | 50mm | 53mm | 53mm |



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

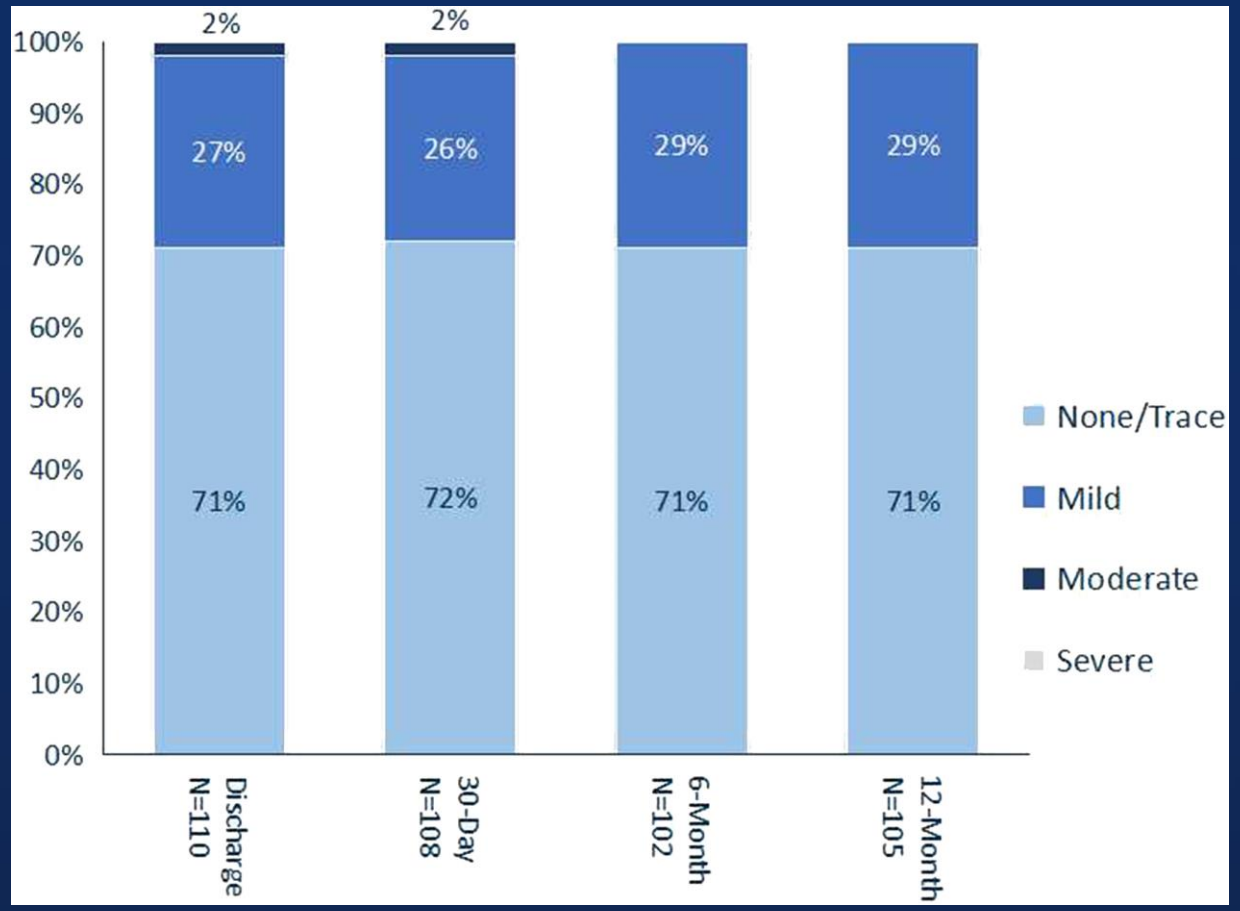





Cathet Cardio Intervent, Volume: 95, Issue: 2, Pages: 332-338

# VitaFlow

No moderate or severe PVL at 12 months

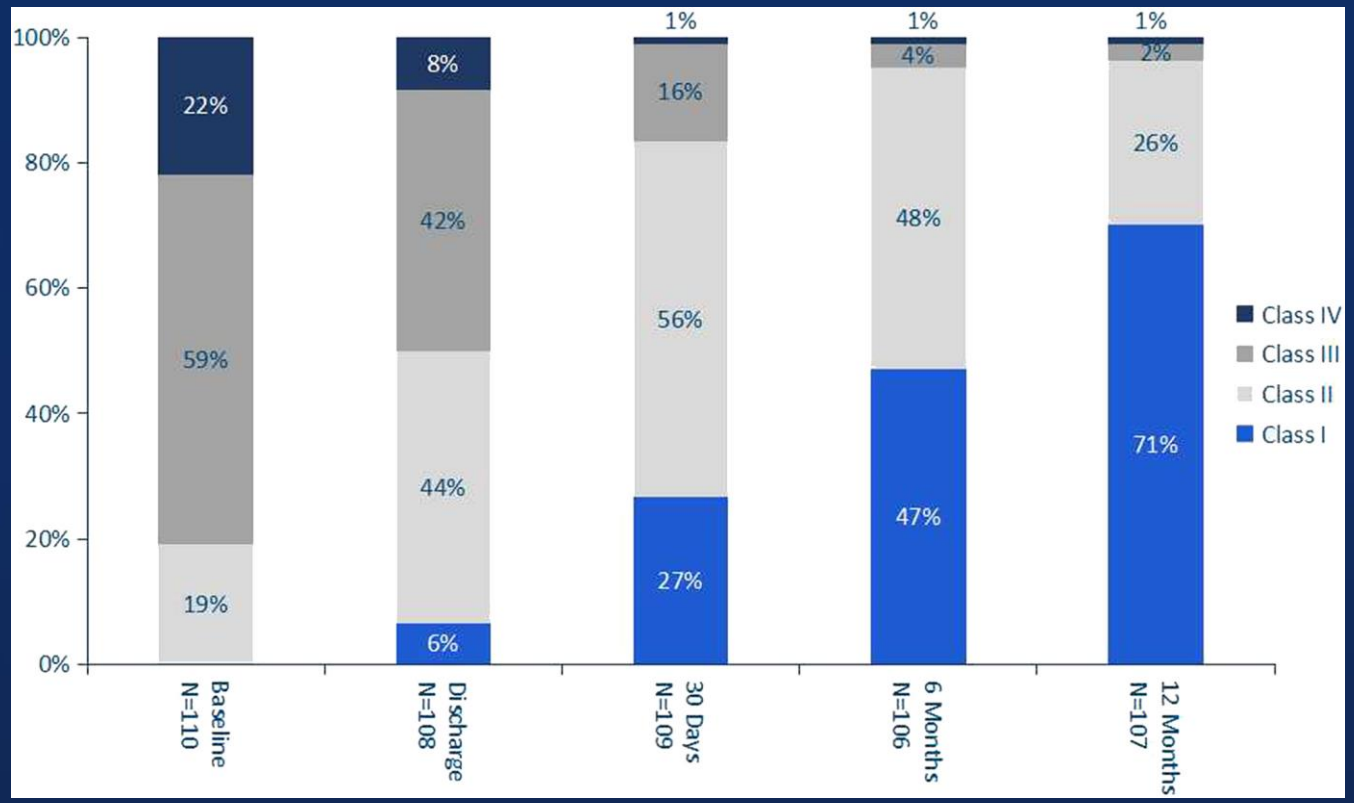





Cathet Cardio Intervent, Volume: 95, Issue: 2, Pages: 332-338

# 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



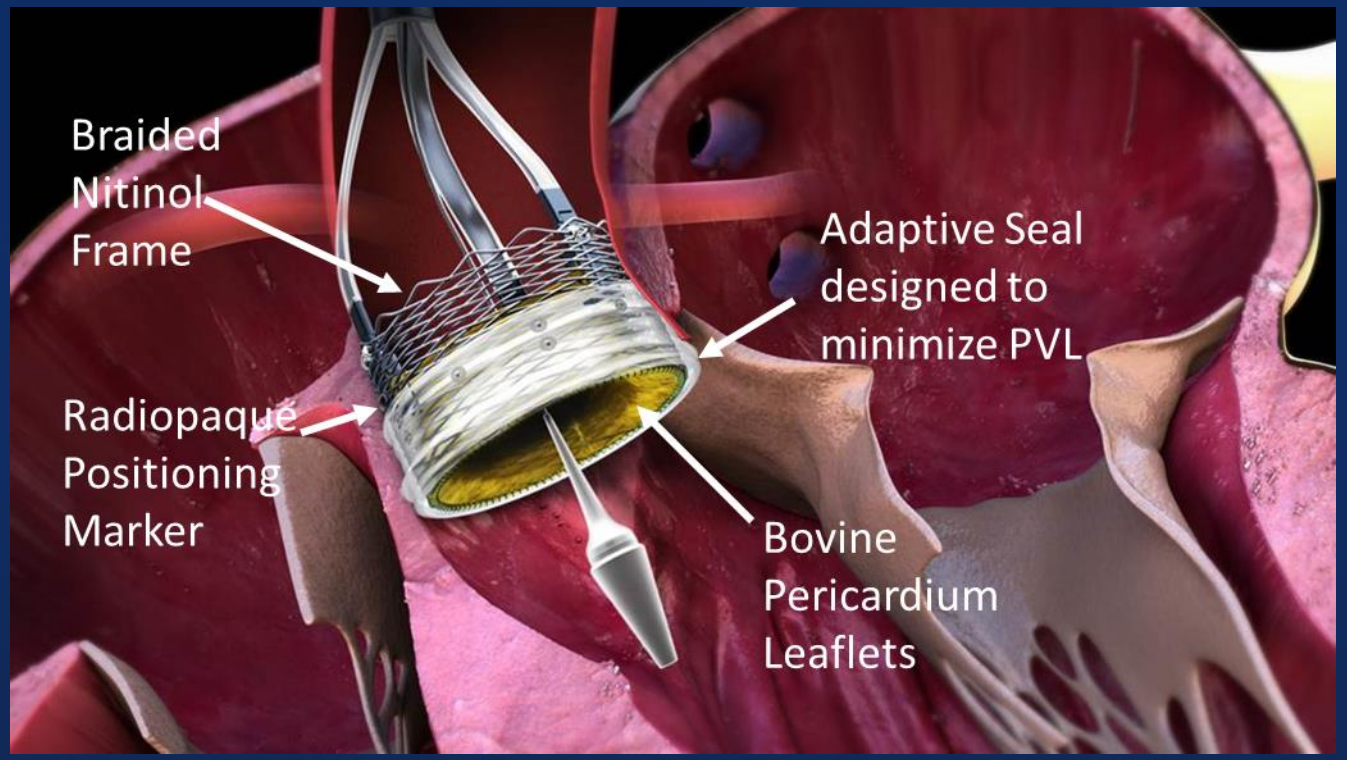
Methodist Debakey Cardiovasc J. 2012 Apr;8(2):9-12

# Direct Flow Medical Aortic valve




# REPRISE III

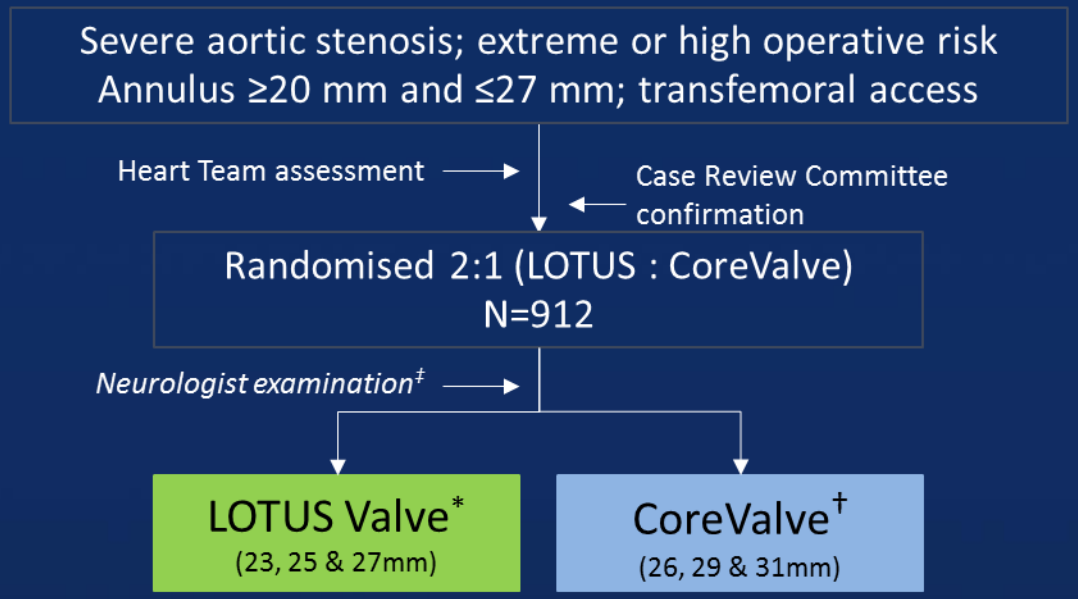
# The LOTUS Valve




- 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




- 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

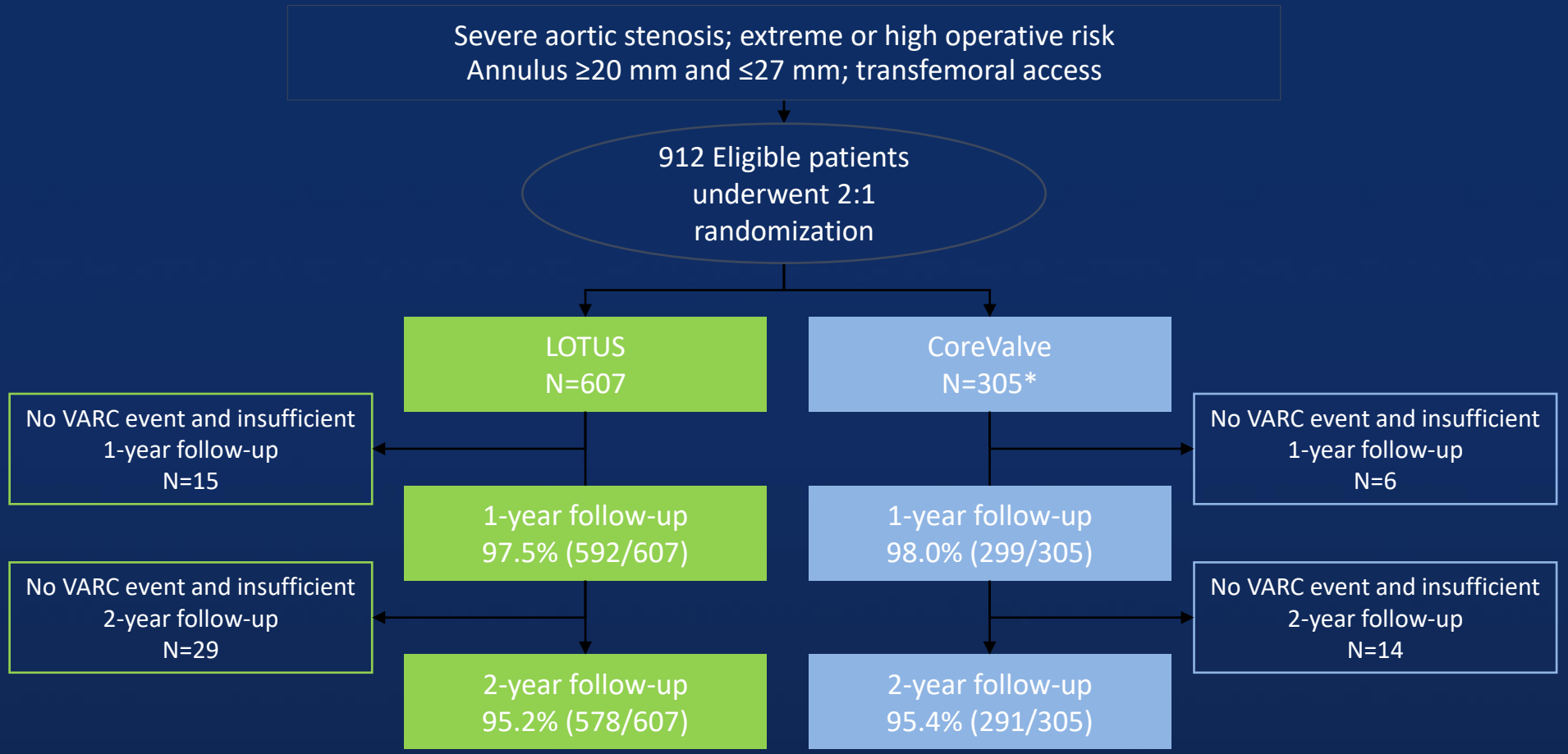
Driven by significant differences in ≥moderate PVL (CoreValve 6.8% vs LOTUS 0.9%, P<0.001) and disabling stroke (7.1% vs 3.6%, P=0.02)



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

REPRISE III
Lotus Valve System

# 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) |



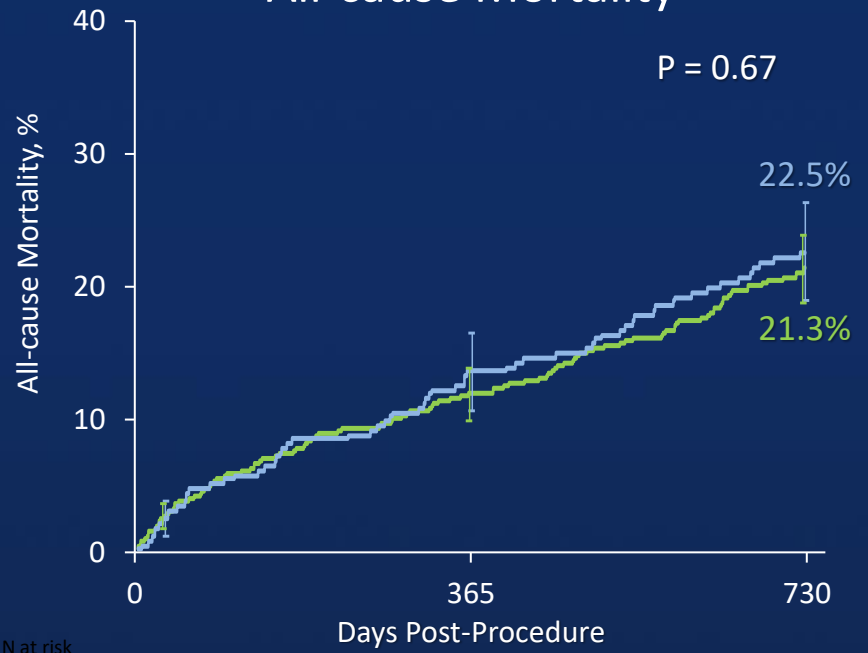
1Feldman TE, Reardon MJ, Rajagopal V,, et.aAl.. JAMA. 2018;319:27–37.

# Key Endpoints – REPRISE III

*2 Year – Intent-to-Treat*

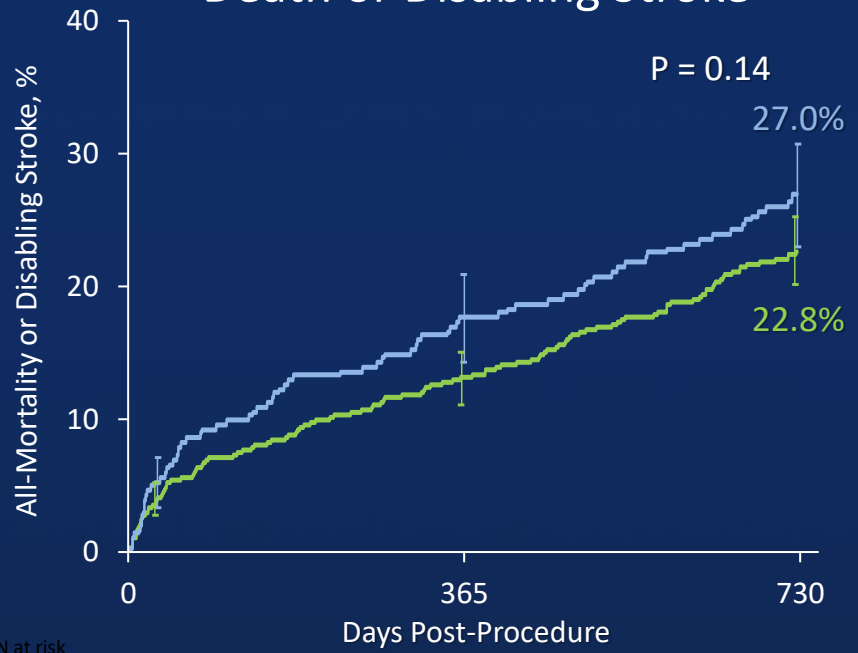
CoreValve
LOTUS

## 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

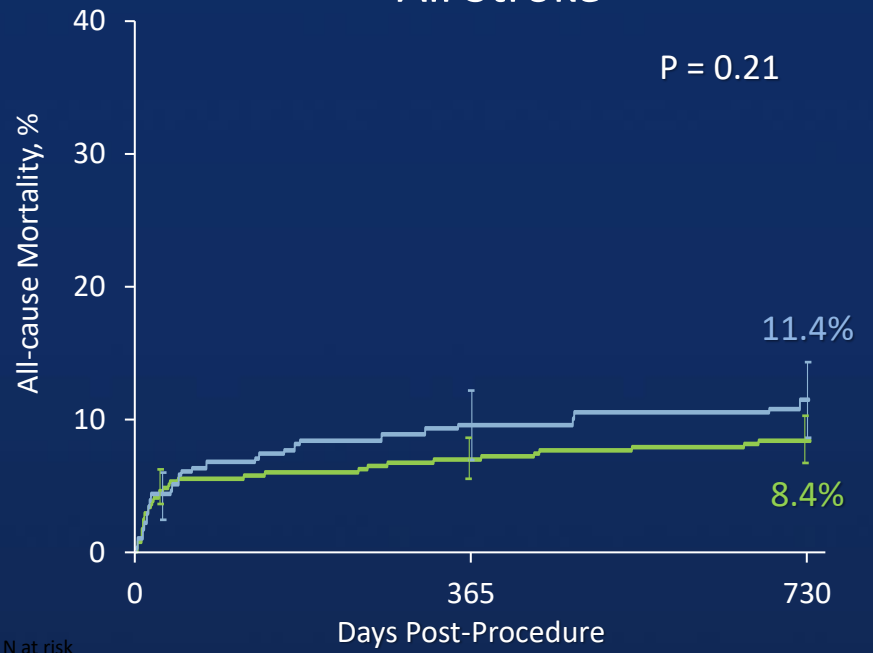
REPRISE III
Lotus™ Valve System

# Other Clinical Outcomes

*2 Year – Intent-to-Treat*

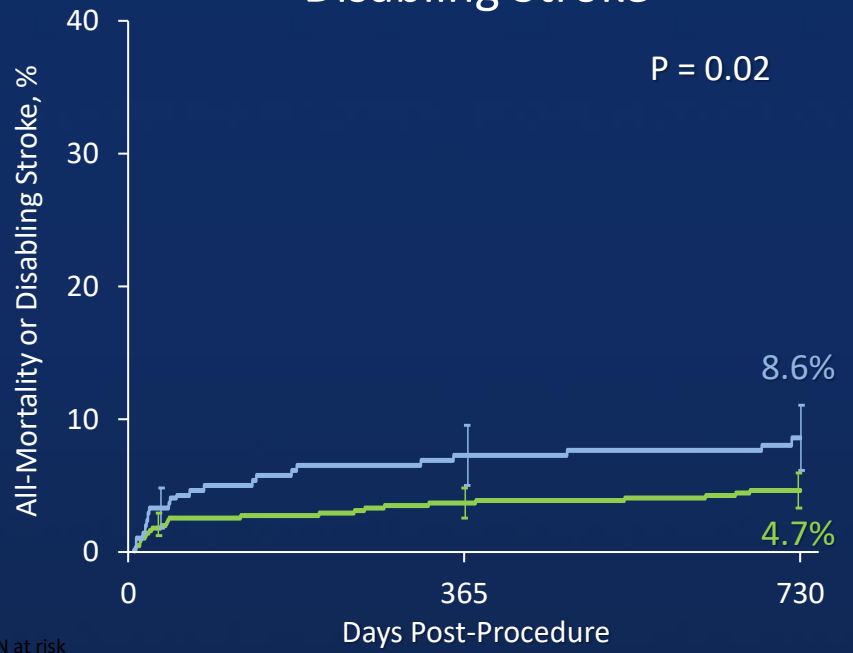
CoreValve
LOTUS

## All Stroke




| N at risk | | | |
|---|---|---|---|
| CoreValve | 282 | 235 | 145 |
| LOTUS | 558 | 488 | 325 |

## Disabling Stroke



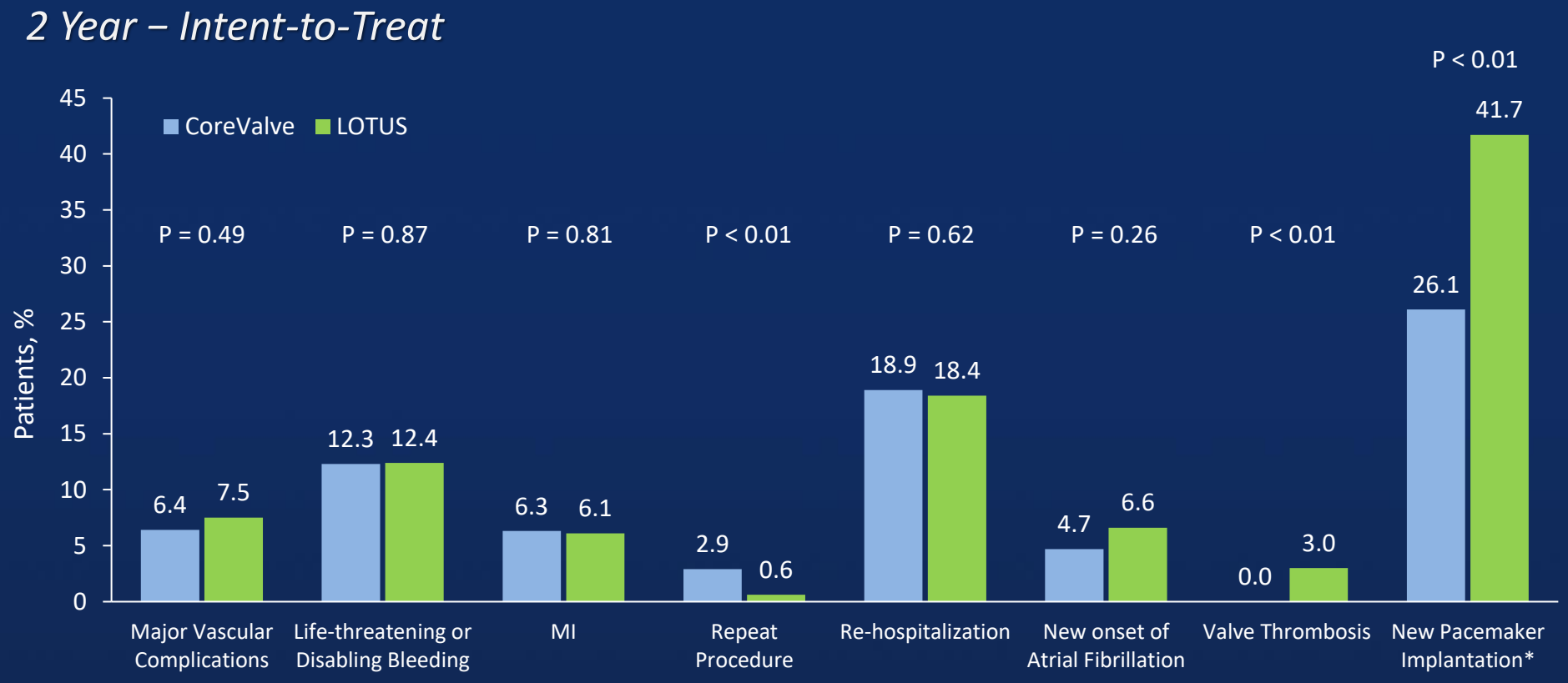

| N at risk | | | |
|---|---|---|---|
| CoreValve | 297 | 248 | 186 |
| LOTUS | 588 | 517 | 403 |

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);

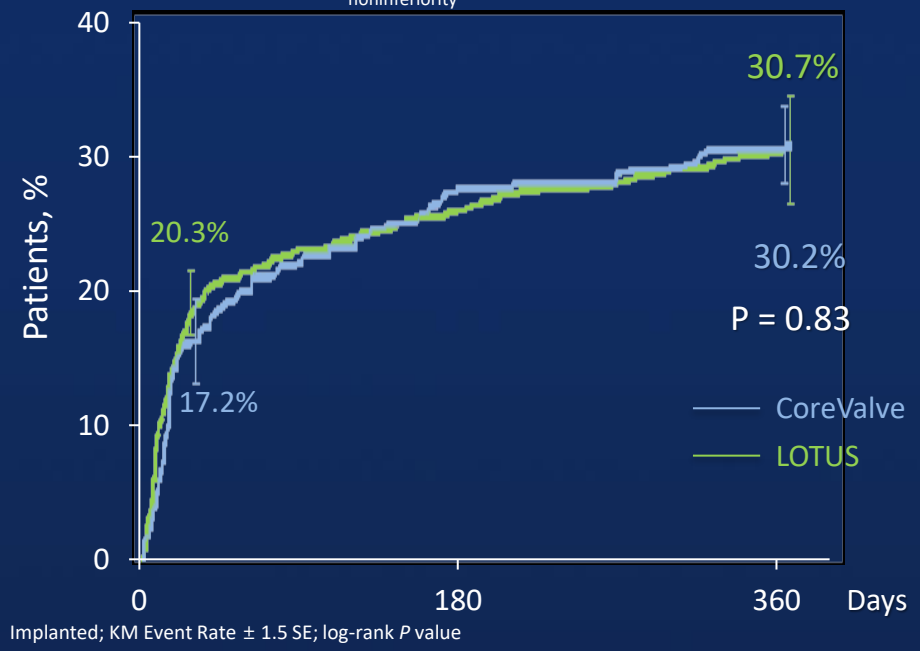
# REPRISE III – Primary Results

## Primary Composite Safety Endpoint

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

✓ Satisfied noninferiority

$P_{noninferiority} = 0.003$



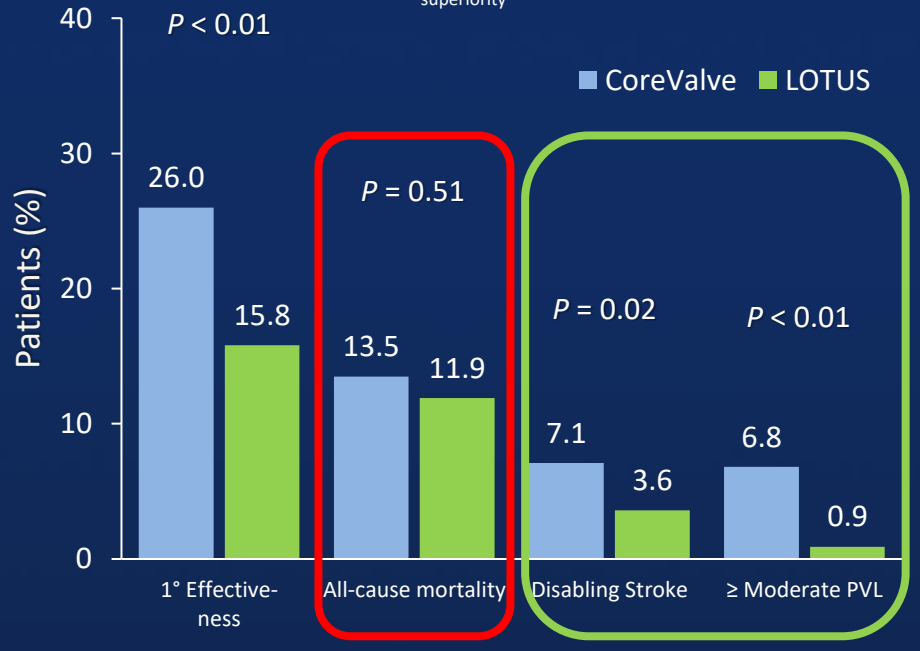

Implanted; KM Event Rate ± 1.5 SE; log-rank *P* value

## 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

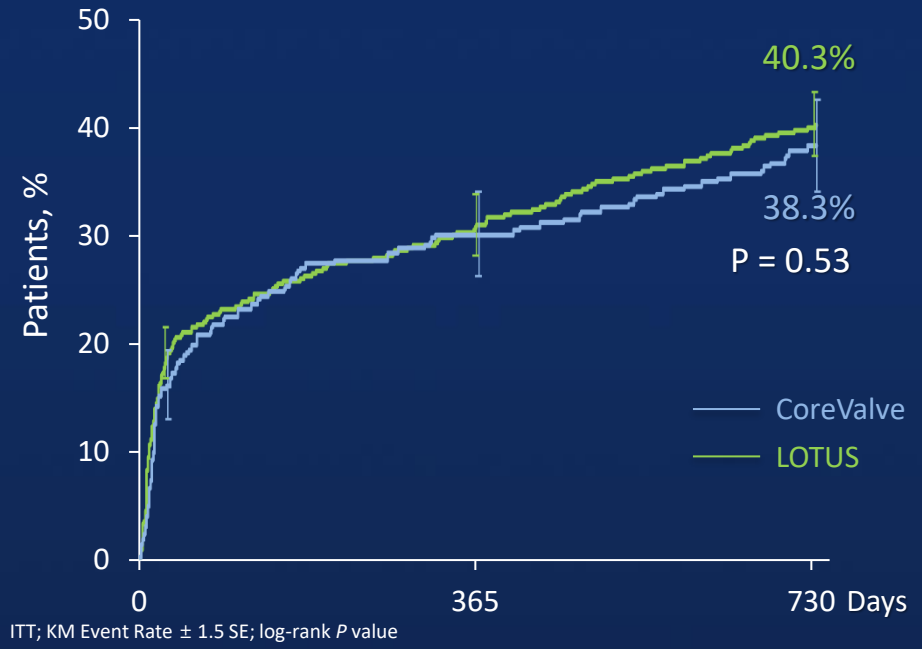
REPRISE III
Lotus™ Valve System

# Primary Safety and Effectiveness at 2 years

*Intent-to-Treat*

## Primary Composite Safety Endpoint

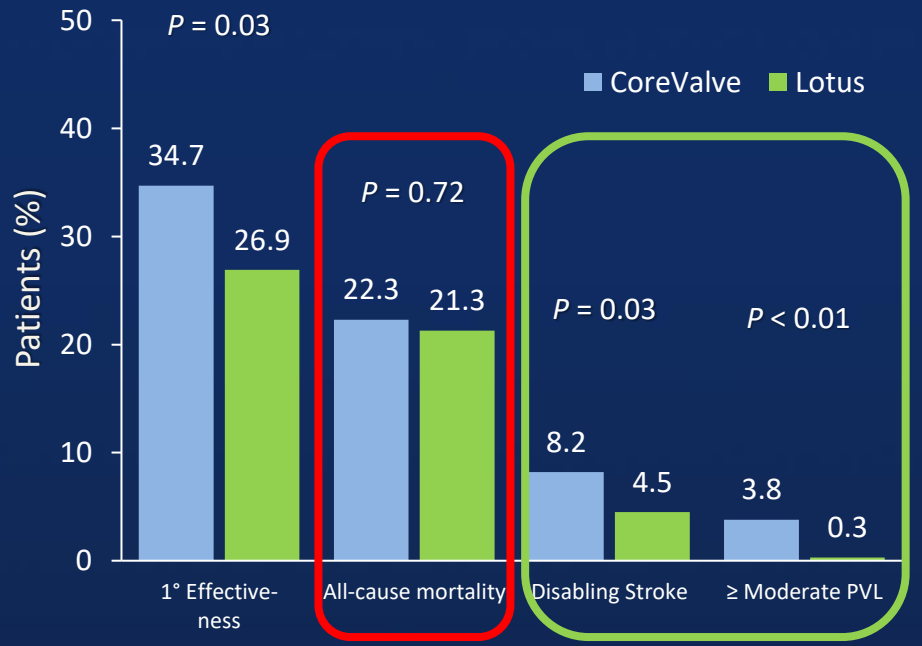
*All-cause mortality, stroke, life-threatening/major bleed, stage 2/3 AKI, major vascular complications*




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

## Primary Effectiveness Endpoint

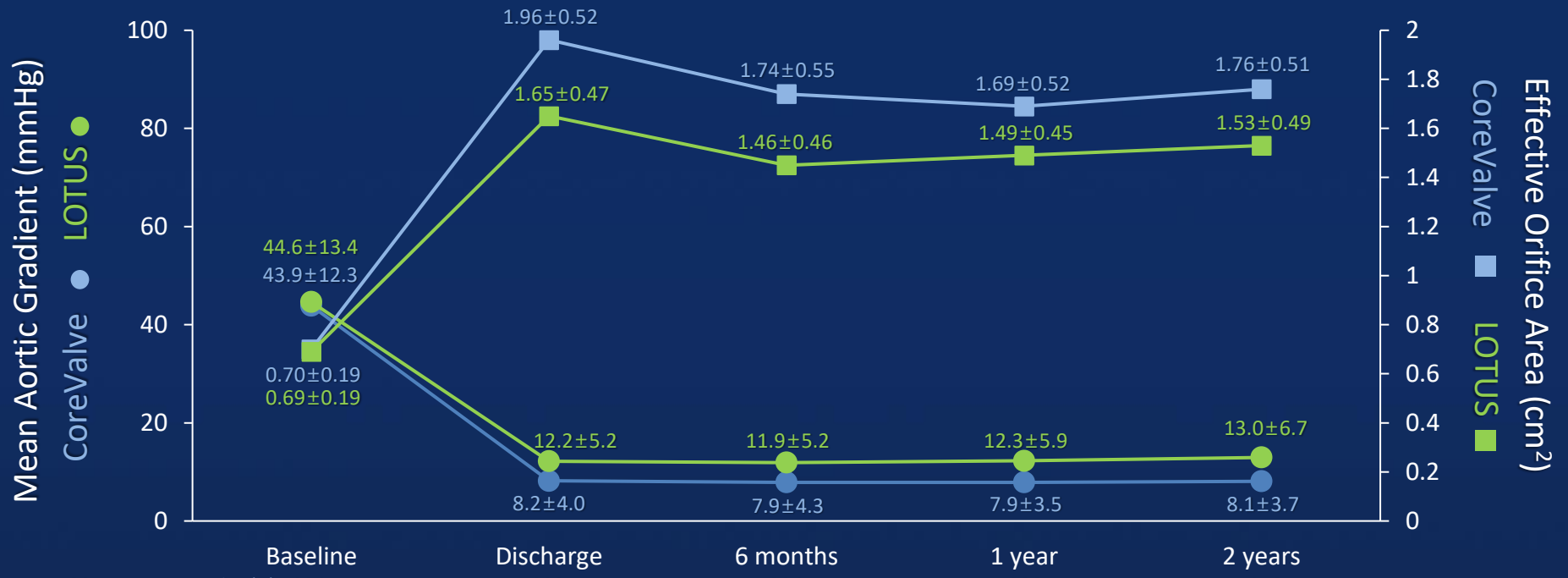
*Death, Disabling Stroke, Moderate or Greater PVL*




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

# Hemodynamics

*Core Lab Data*



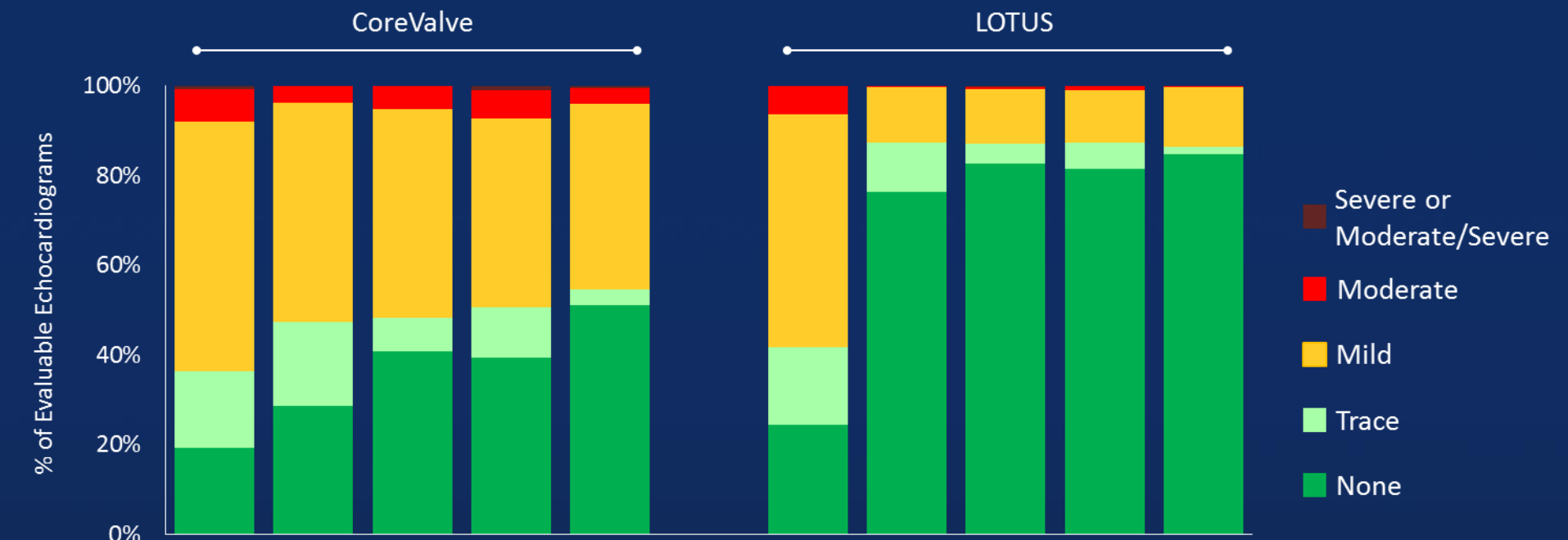

| | | Baseline | Discharge | 6 months | 1 year | 2 years |
|---|---|---|---|---|---|---|
| Mean Gradient | CoreValve (N) | 294 | 280 | 234 | 220 | 176 |
| | LOTUS (N) | 575 | 564 | 485 | 465 | 381 |
| EOA | CoreValve (N) | 280 | 246 | 210 | 200 | 167 |
| | LOTUS (N) | 541 | 510 | 440 | 422 | 326 |

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

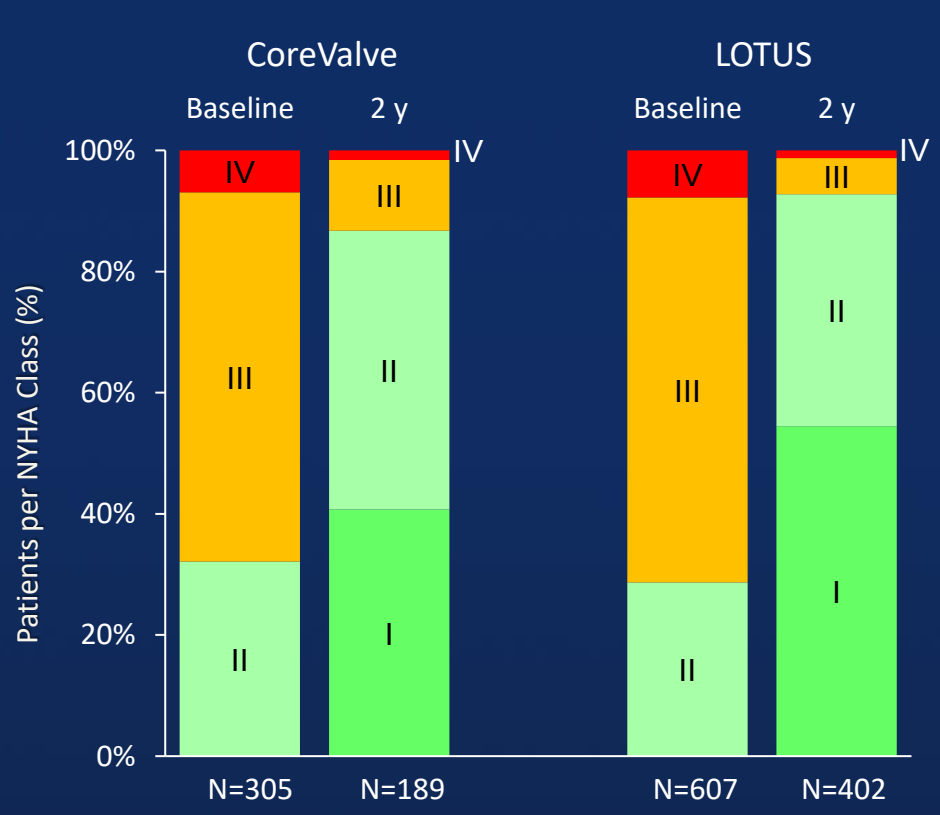
# Regurgitation through 2 years

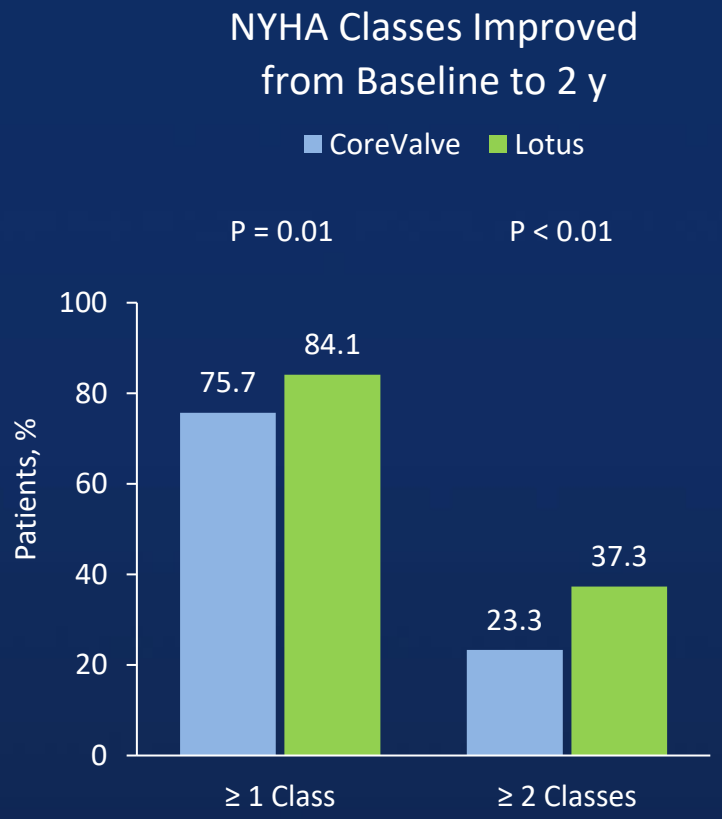



| | CoreValve | | | | | LOTUS | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Base-line | Dis-charge | 6 mo | 1 y | 2 y | Base-line | Dis-charge | 6 mo | 1 y | 2 y |
| | N=289 | N=266 | N=215 | N=205 | N=174 | N=558 | N=529 | N=443 | N=445 | N=352 |
| ≥Moderate Regurgitation | 8.0 | 3.8 | 5.1 | 7.3 | 4.0 | 6.5 | 0.4 | 0.7 | 0.9 | 0.3 |
| P value vs CoreValve: | | | | | | | 0.005 | 0.006 | <0.001 | 0.002 |

Baseline = includes aortic regurgitation only

# Functional Status at 2 years

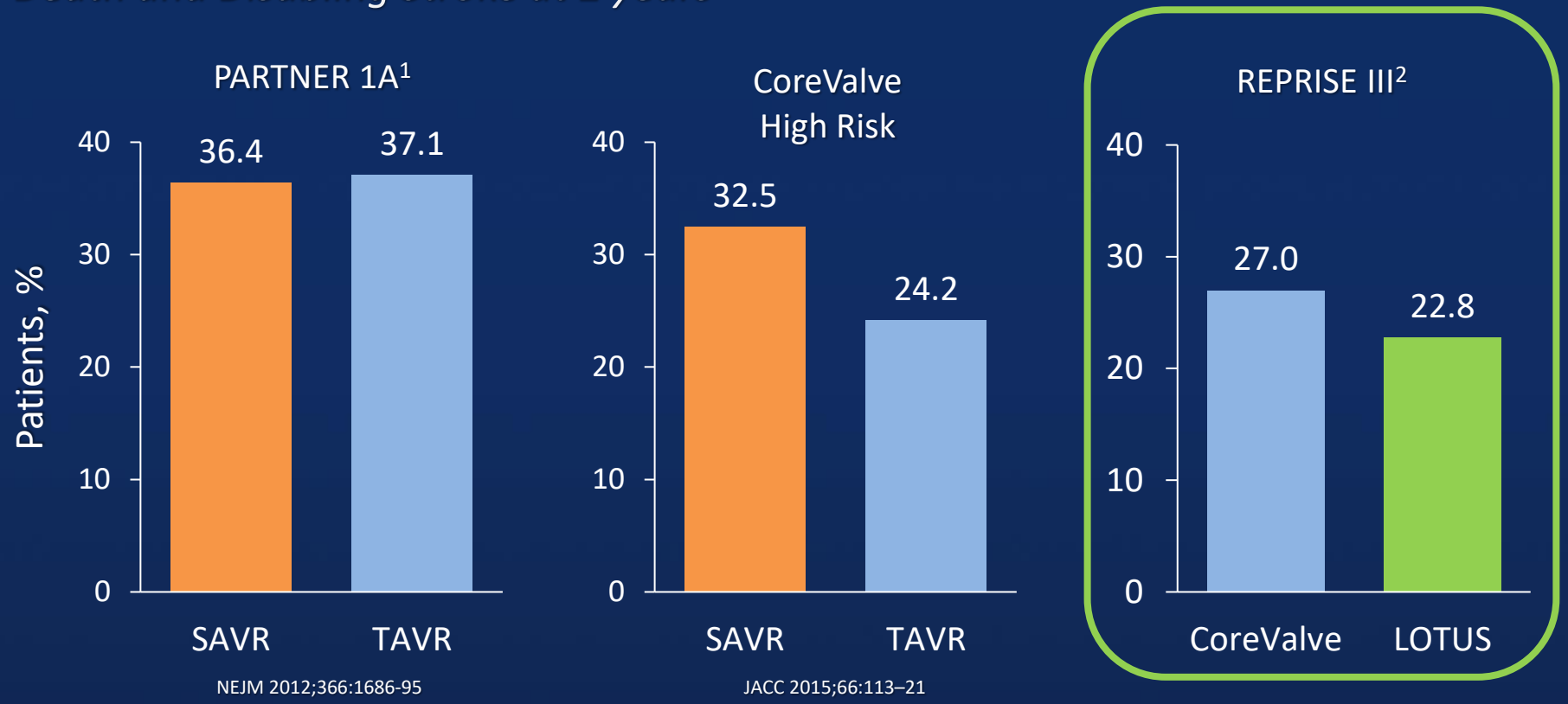


REPRISE III
Lotus™ Valve System

# High Risk TAVR Randomized Trials

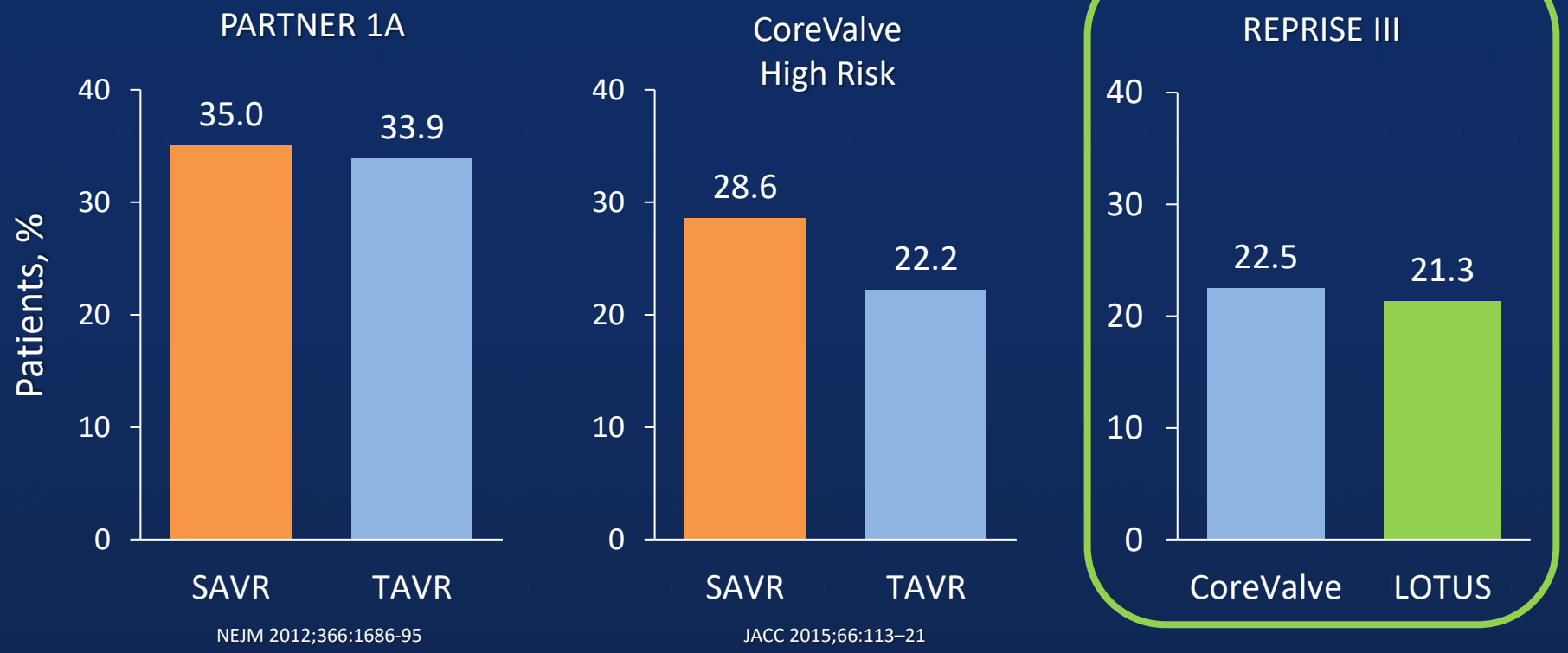
*Death and Disabling Stroke at 2 years*




[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*




NEJM 2012;366:1686-95

JACC 2015;66:113–21

REPRISE III
Lotus™ Valve System

# Conclusions

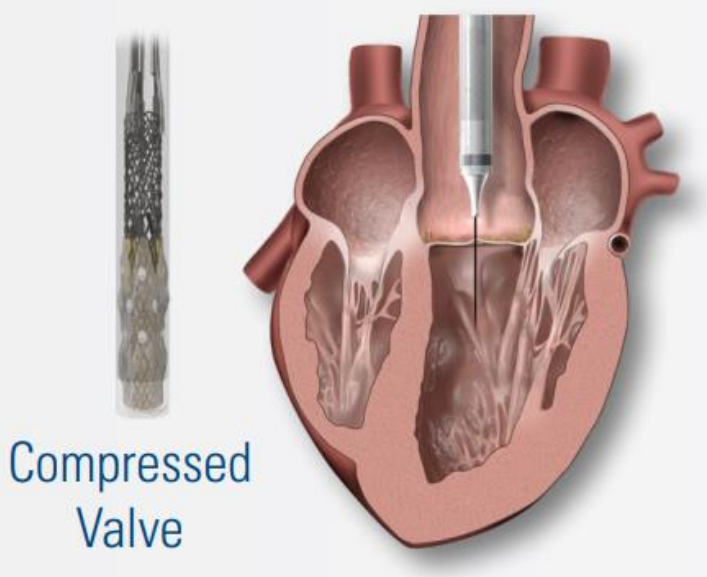
The 2-year findings in REPRISE III continue to demonstrate the safety and effectiveness of the LOTUS valve

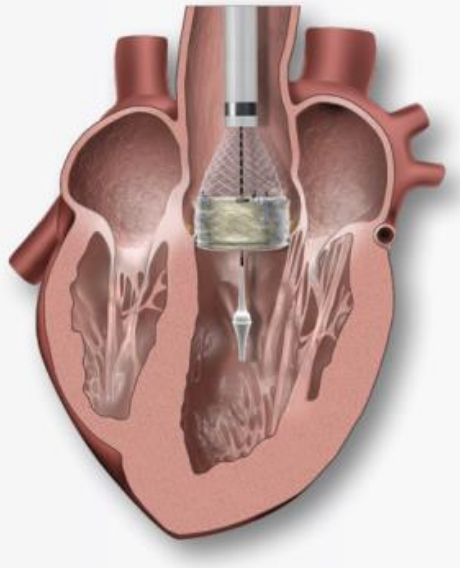
- At 2 years compared to CoreValve LOTUS patients experienced:
  - Less moderate or greater paravalvular leak
  - Fewer disabling strokes
  - Fewer repeat procedures
  - More valve thrombosis
  - More new pacemaker implantations
  - Smaller valve areas and higher gradients
- At 2 years, more LOTUS patients 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

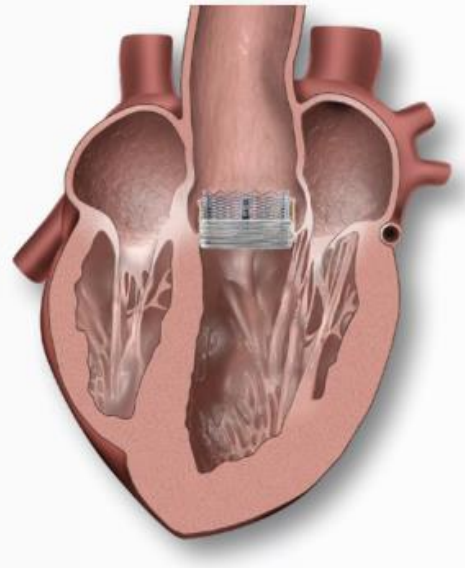
# The LOTUS *Edge*™


- 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**

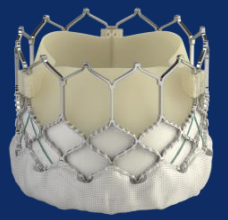
The new valve begins to function immediately and restore healthy blood flow. Once the valve is in place, the physician removes the catheter, closes the incision, and the procedure is complete

# 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 |

| 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

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

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



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# 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.



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# 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%) |



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# 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%)** |

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# 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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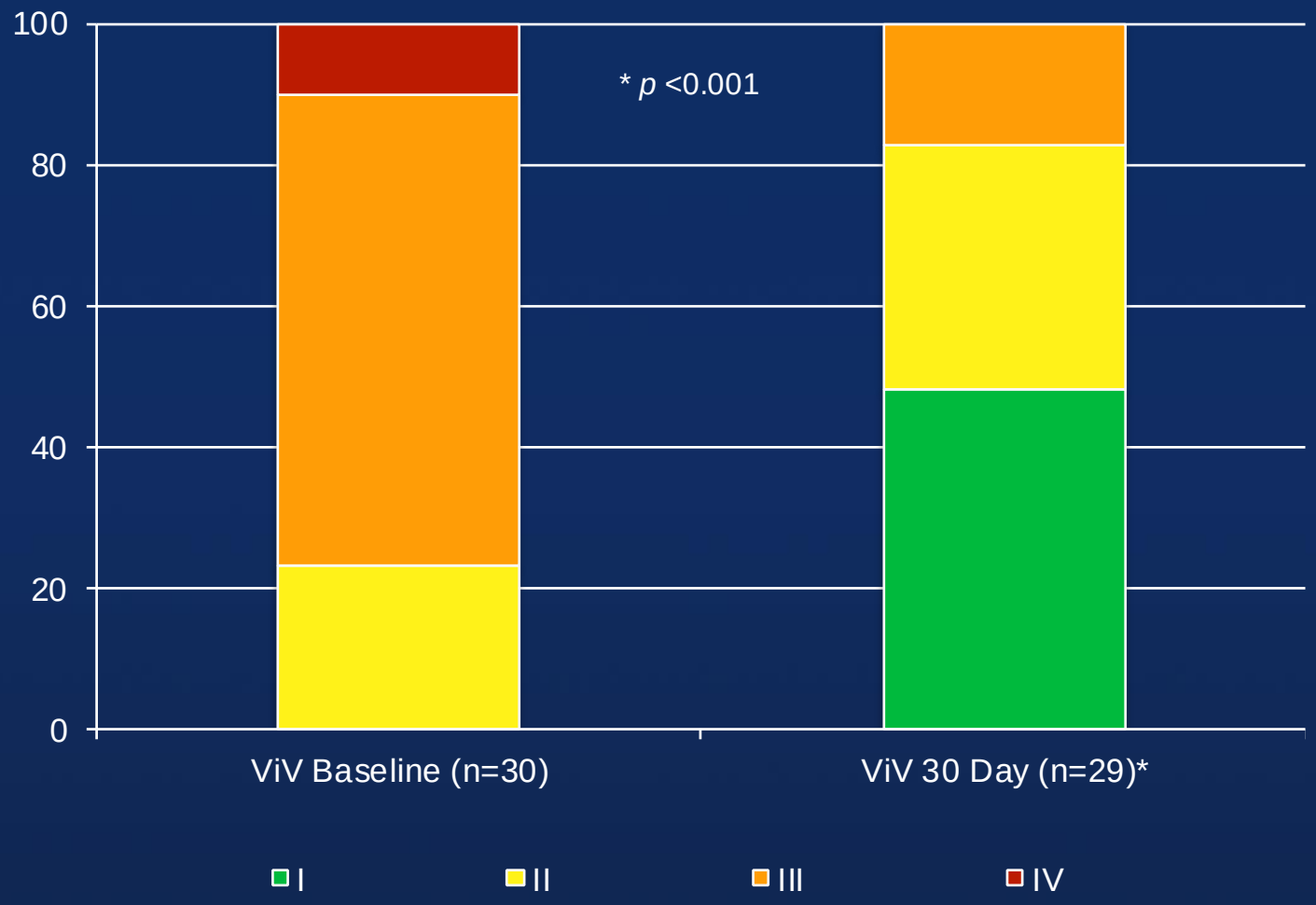
# MITRAL Trial

## NYHA Class at 30 days




1 patient died on POD #29

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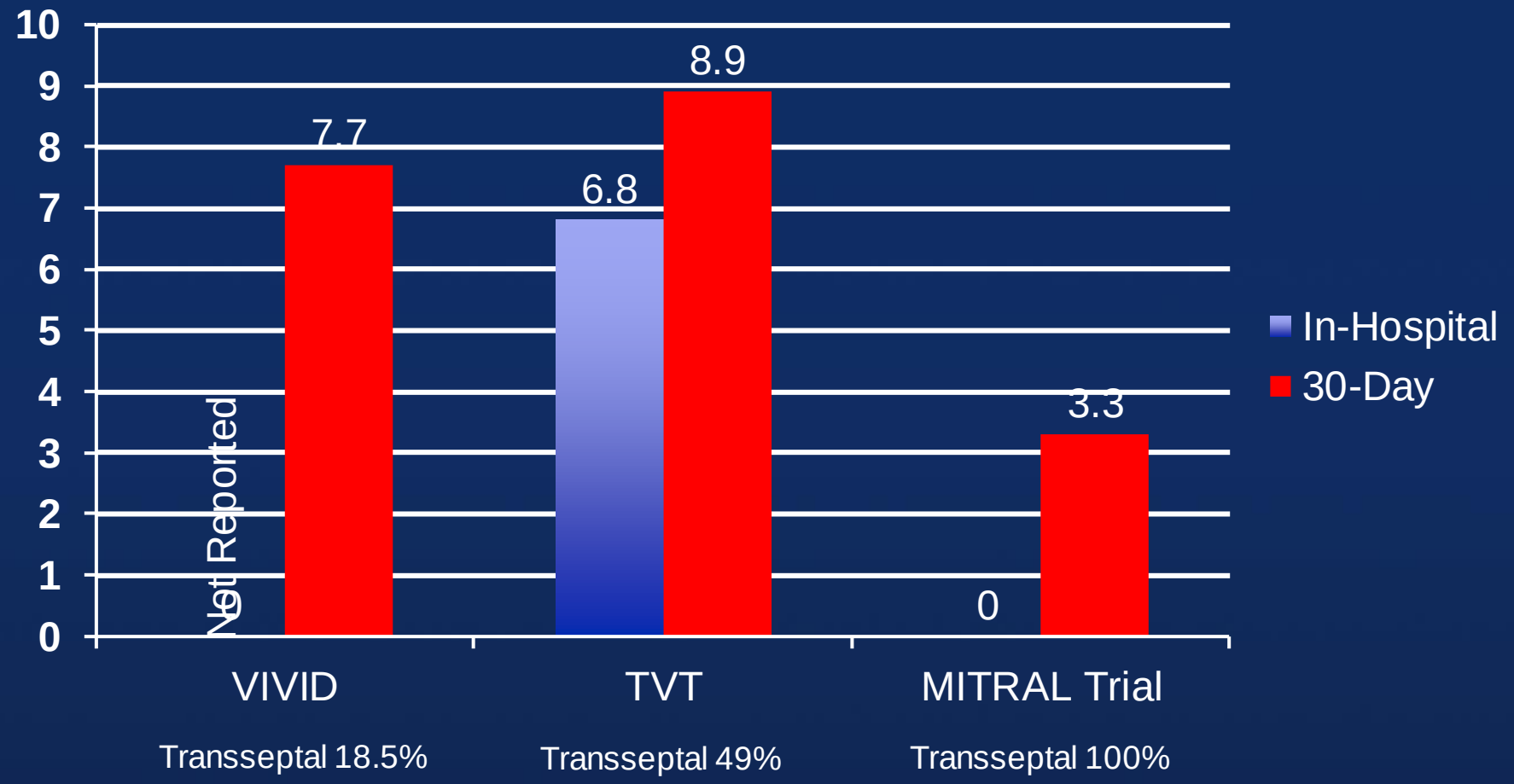
# Mitral ViV All-cause Mortality

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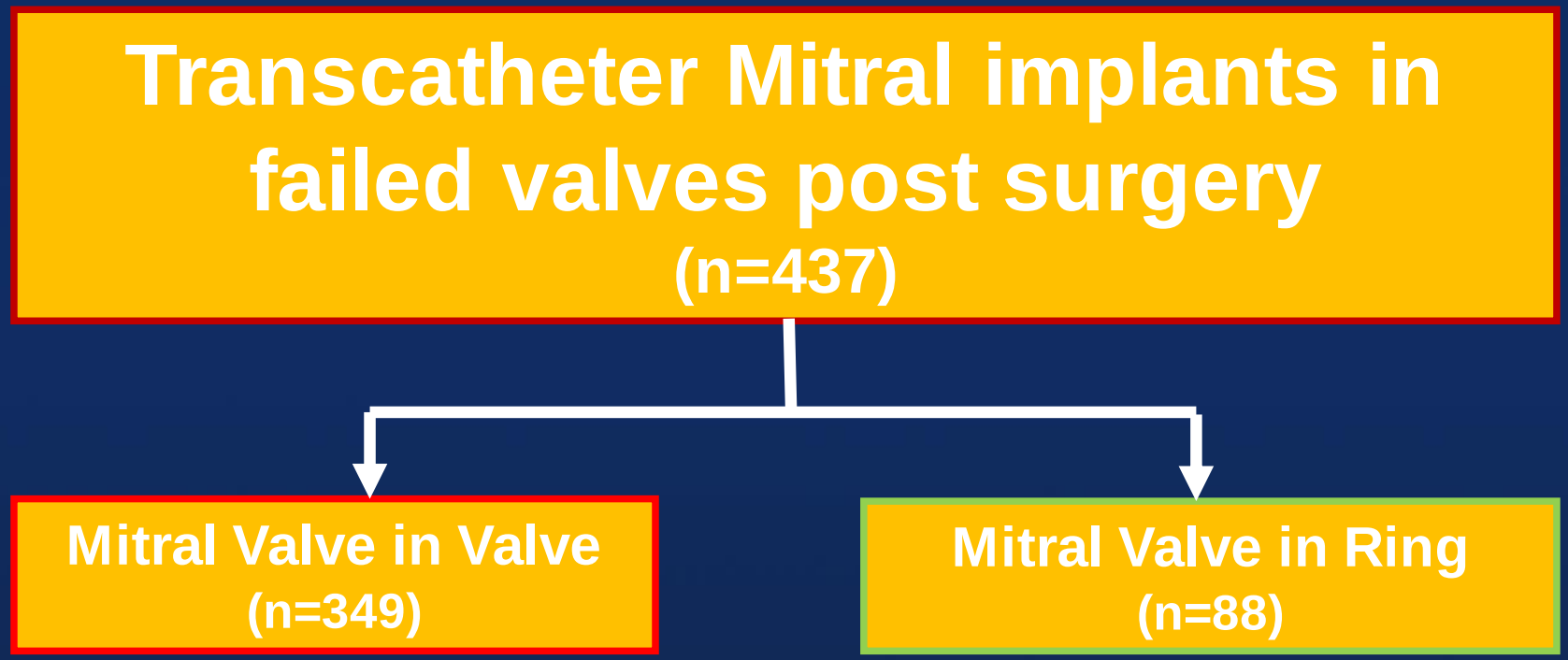
# VIVID Registry

**Median follow up : 408 days**



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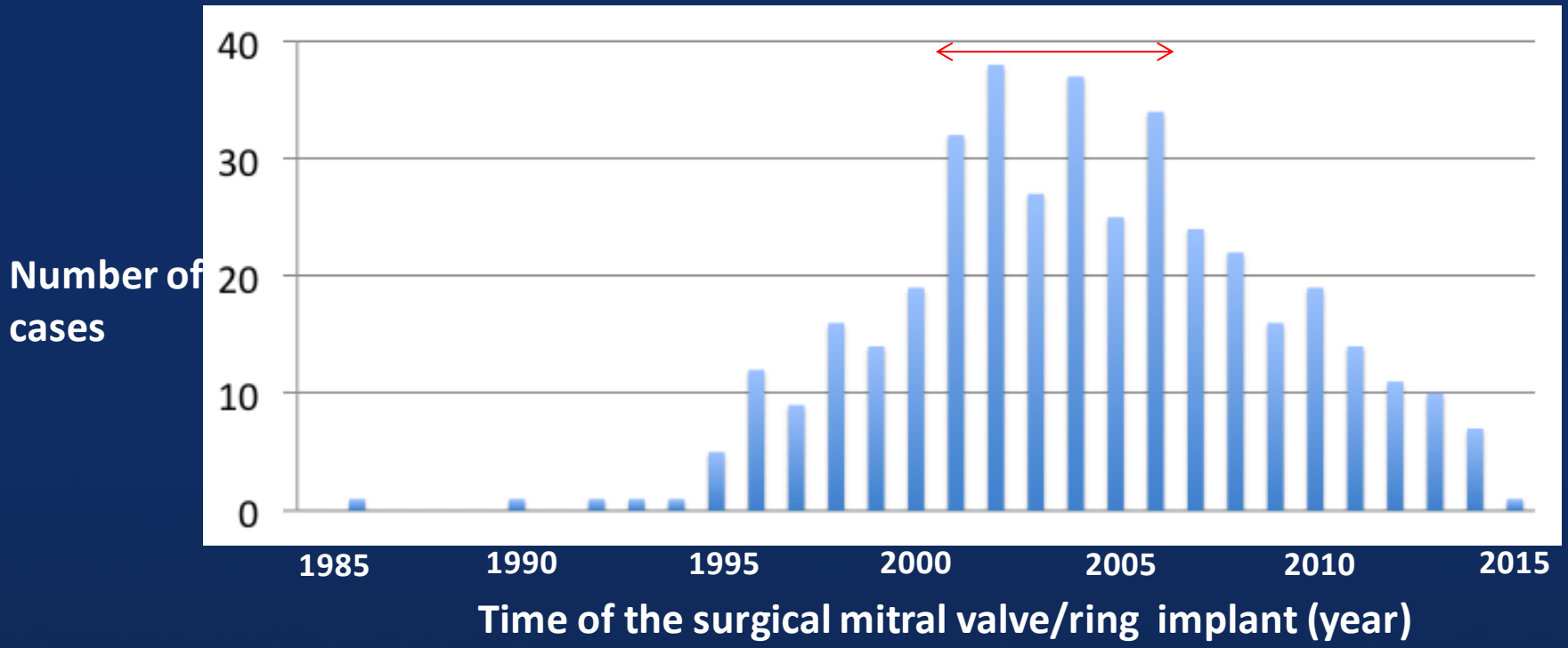
# Index Cardia Surgery

•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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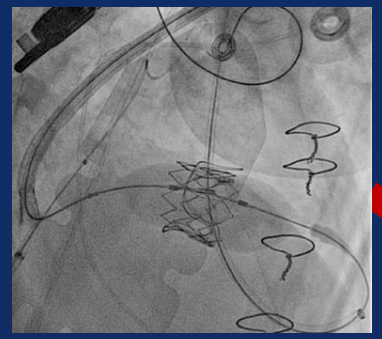
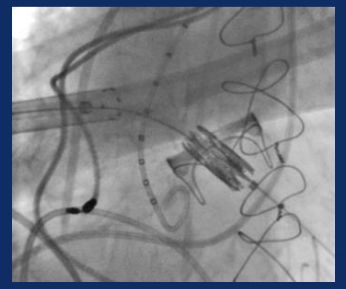
# VIVID Registry

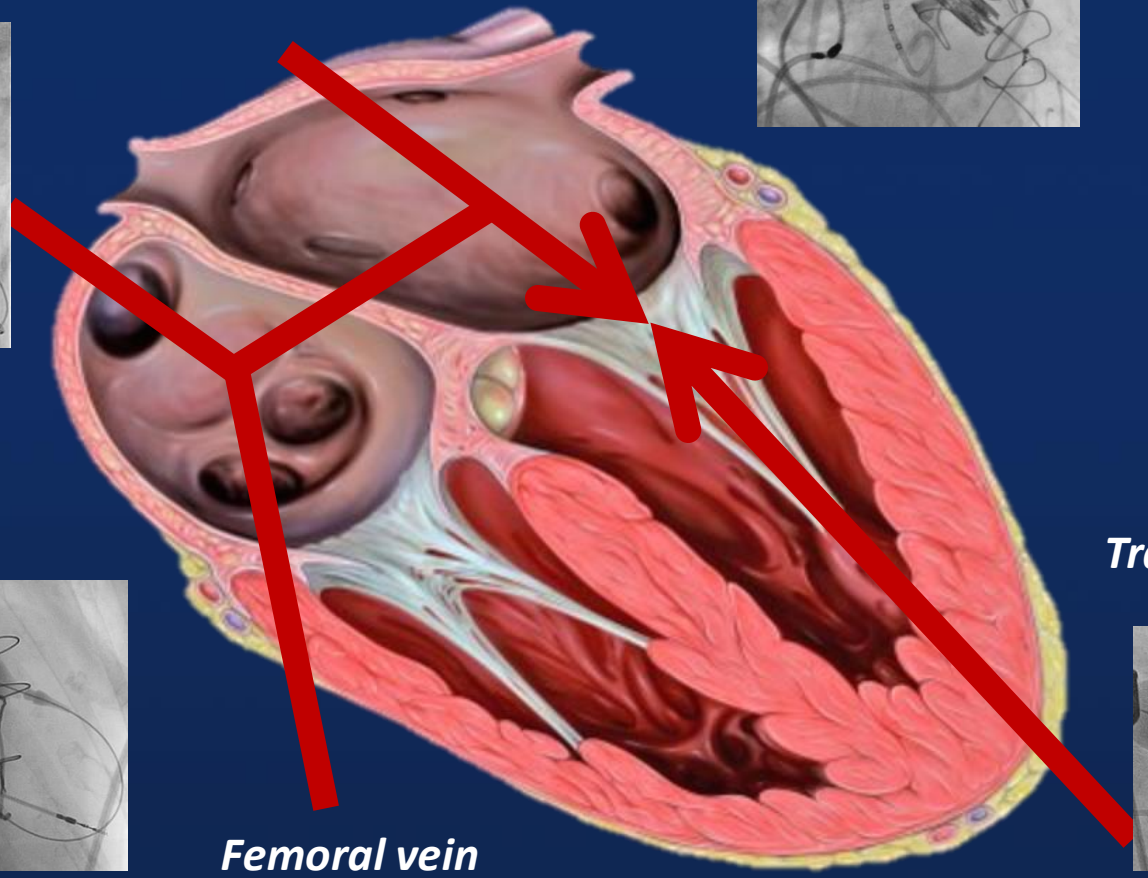
## Access during Mitral ViV procedure

*Jugular Vein*

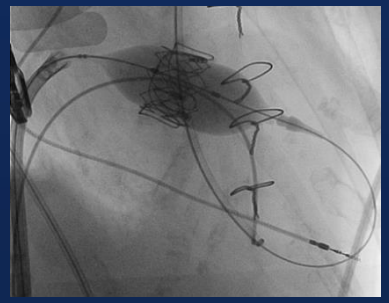


*Direct left atrium*

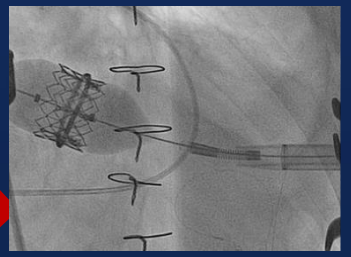




*Total trans-septal*



*Transapical*



*Femoral vein*

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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 |

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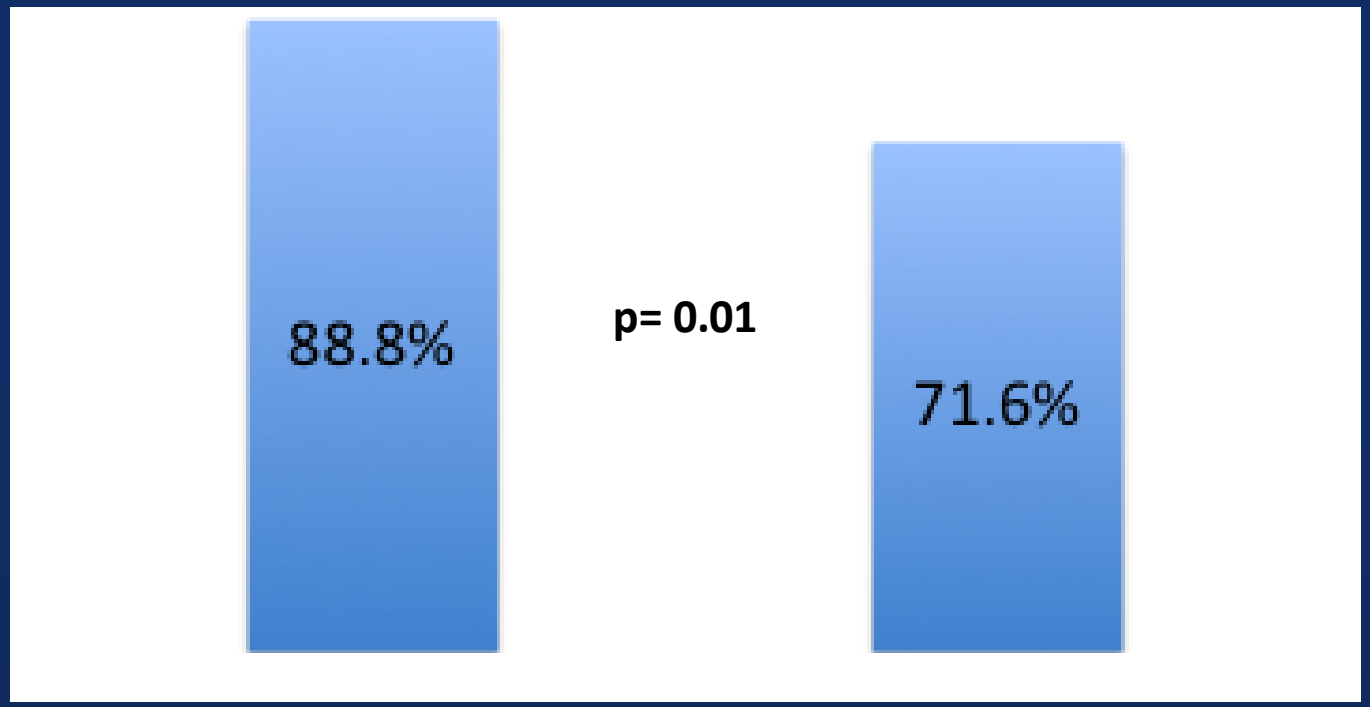
# VIVID Registry

## 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.



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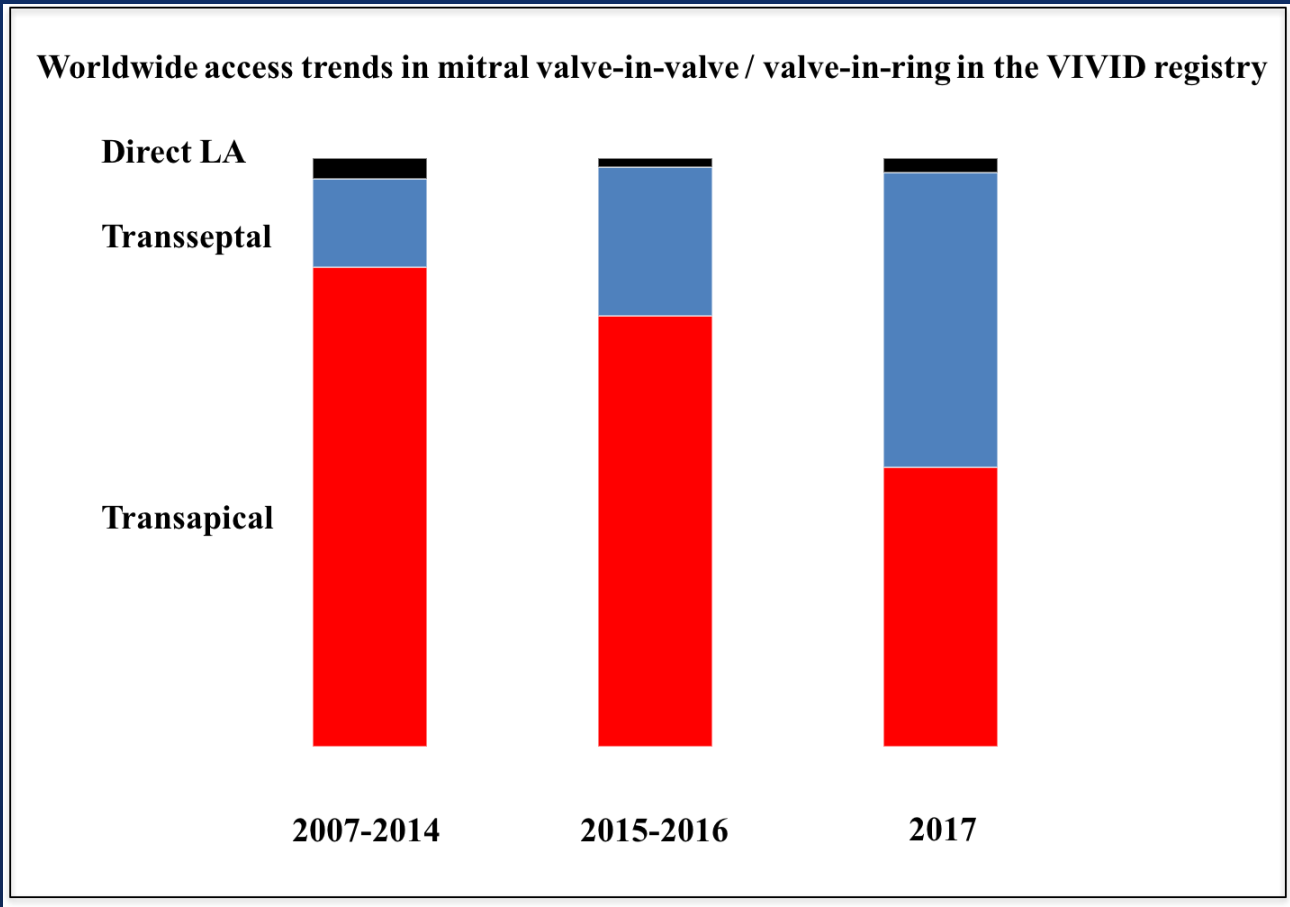
# VIVID Registry




**Transseptal SAPIEN 3 MViV is currently the most common approach**

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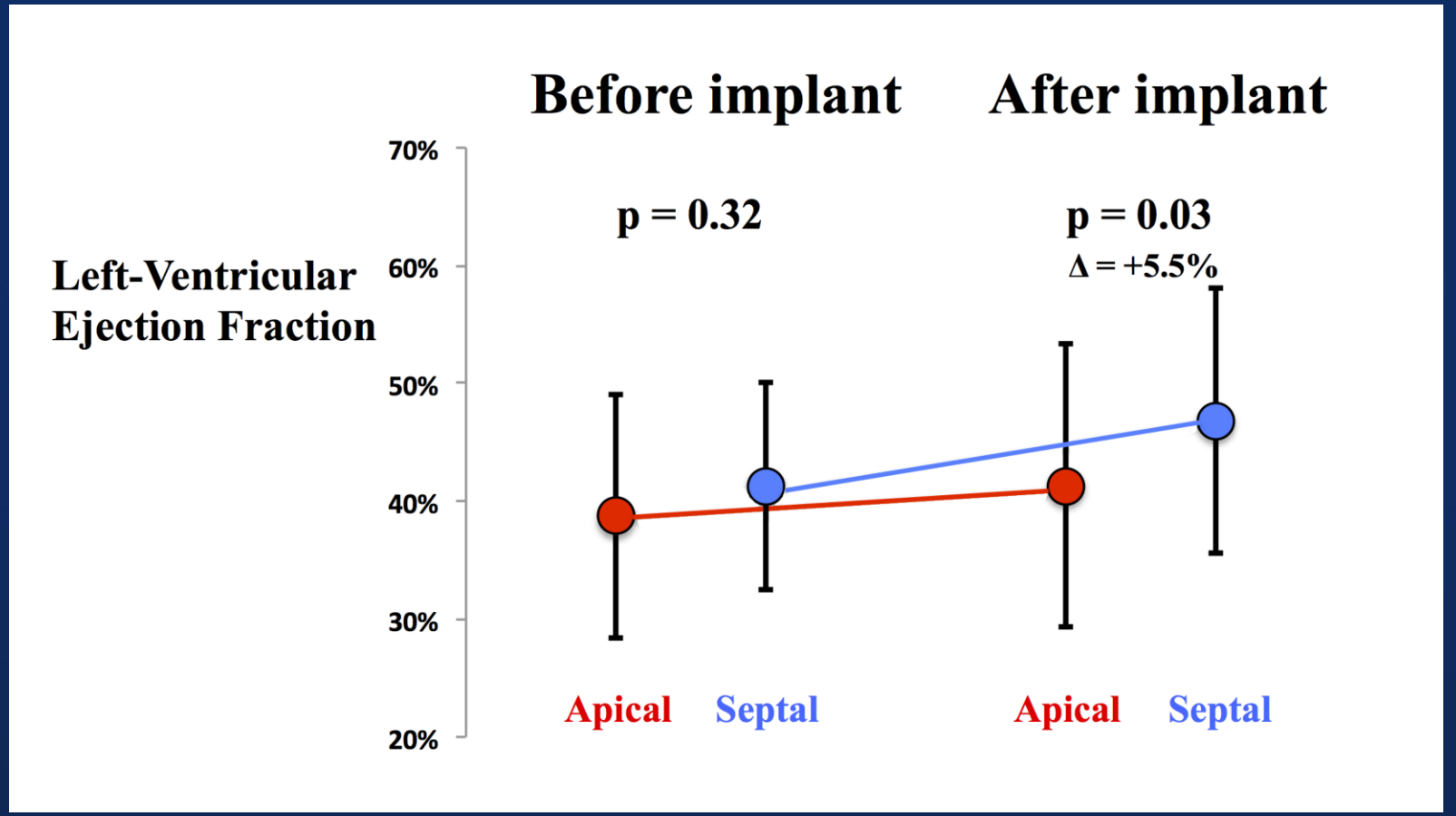
# LV function according to access route




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

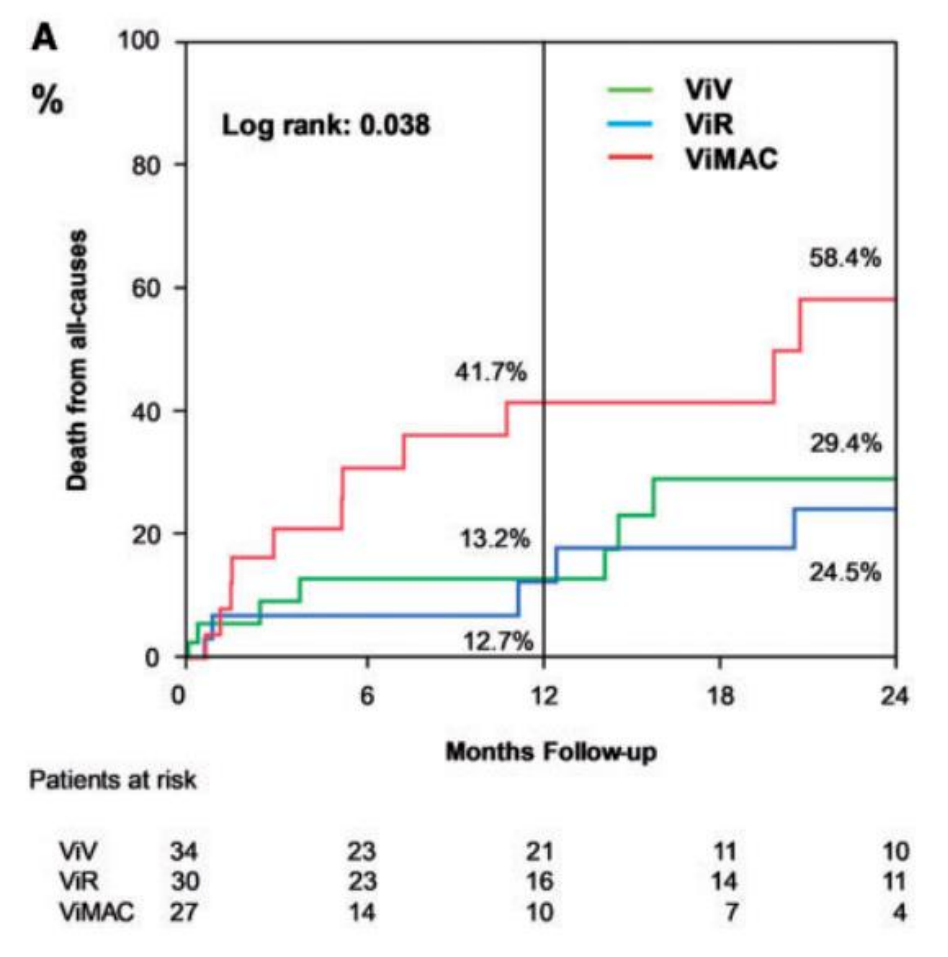
| | Entire cohort ($n = 91$) | Valve-in-valve ($n = 34$) | Valve-in-ring ($n = 30$) | Valve-in-MAC ($n = 27$) | *P*-value |
|---|---|---|---|---|---|
| Death | | | | | |
| *n* (%) | 30 (33.0) | 8 (23.5) | 10 (33.3) | 12 (44.4) | |
| HR (95% CI) | | 1.0 | 0.82 (0.29–2.31) | 2.39 (1.01–5.86)[a] | 0.046 |
| 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.

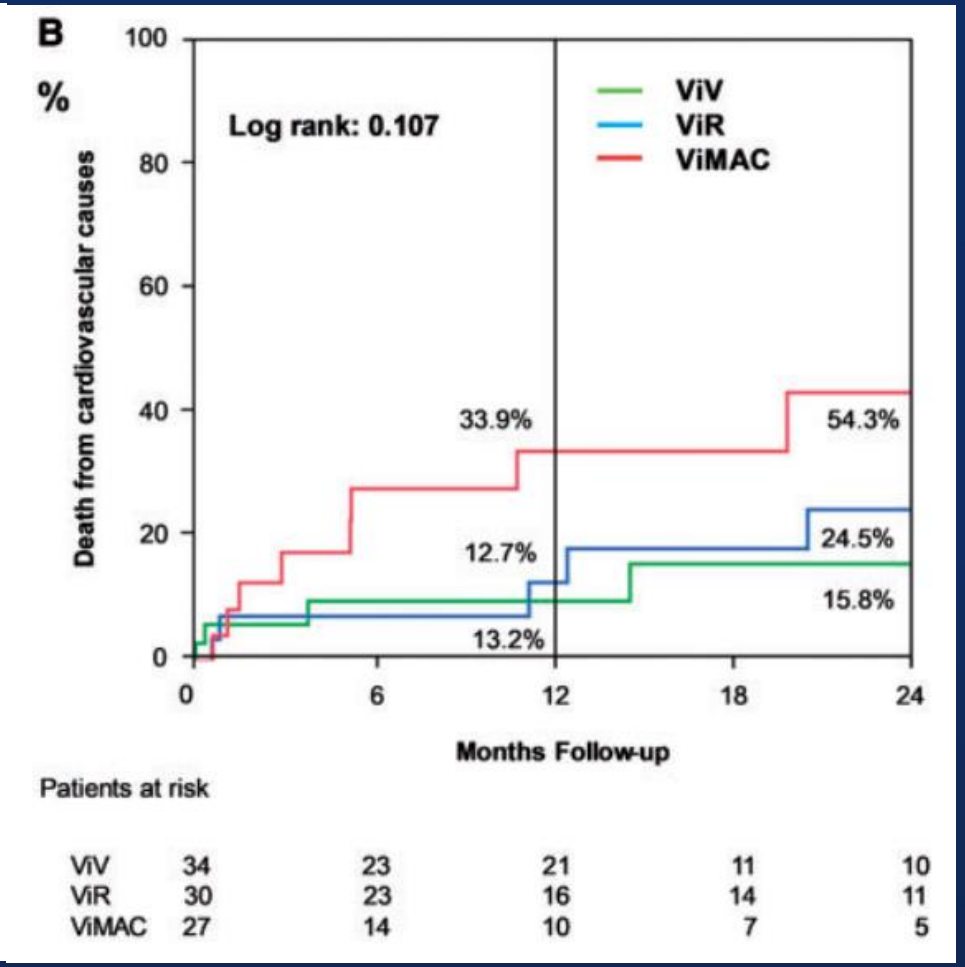
Marina Urena. EHJ 2018.

# Transcatheter MVI: 7-year experience

## All cause death



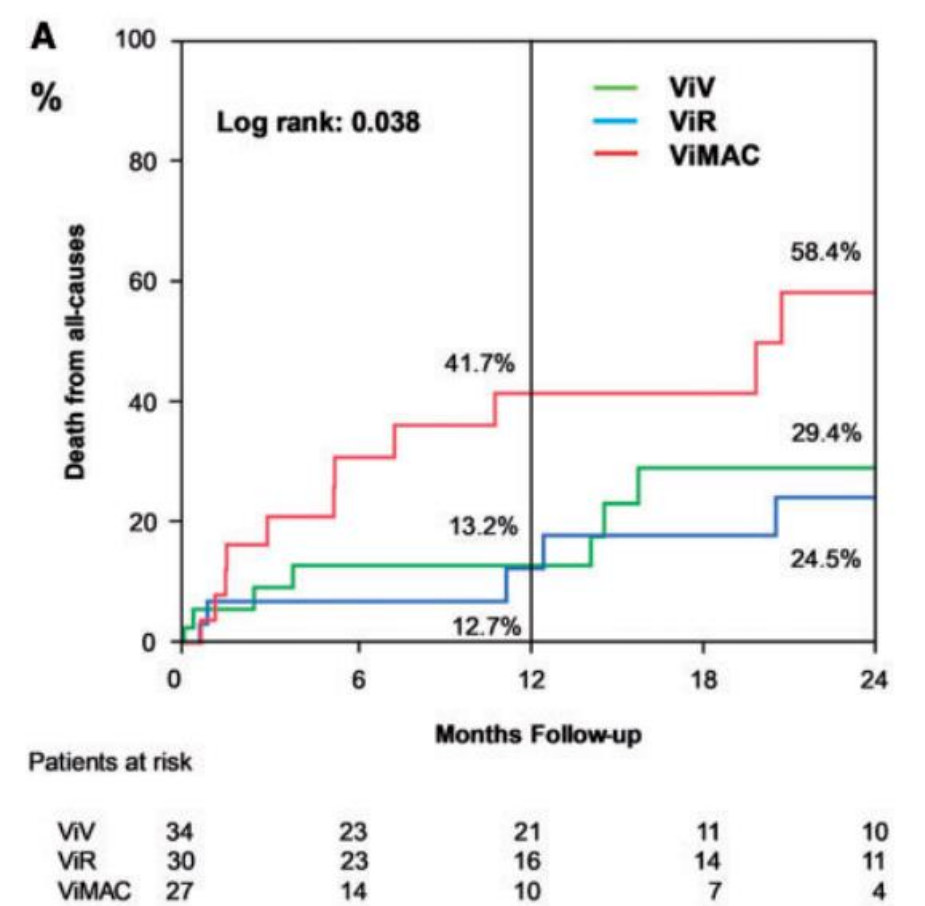

## CV death



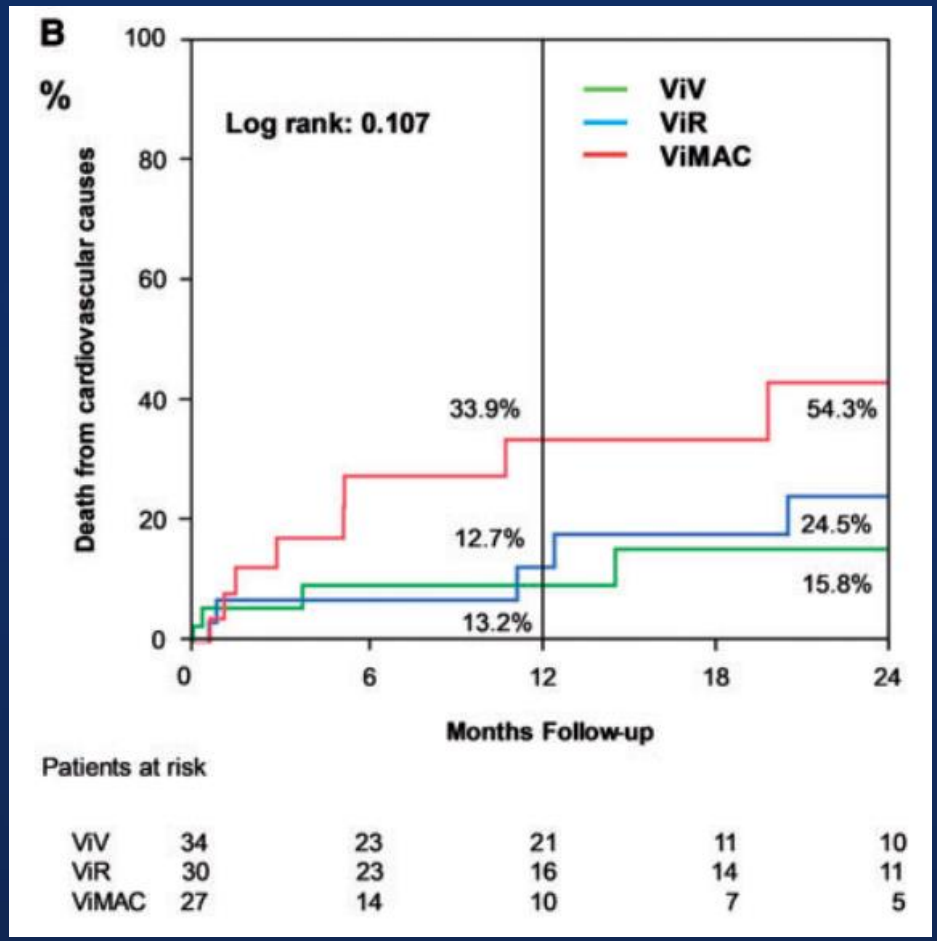

Marina Urena. EHJ 2018.

# Transcatheter MVI: 7-year experience

## All cause death



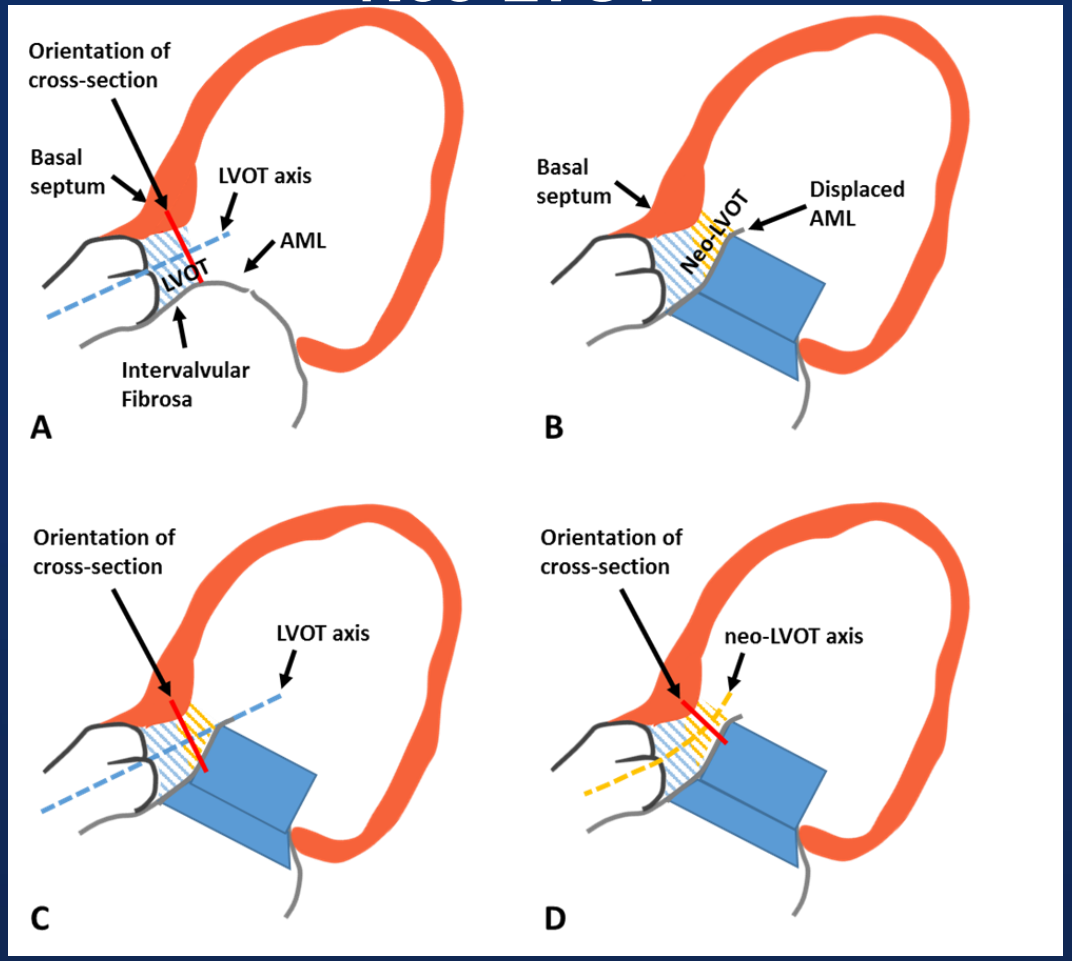

## CV death




Marina Urena. EHJ 2018.

# Prediction of LVOT obstruction

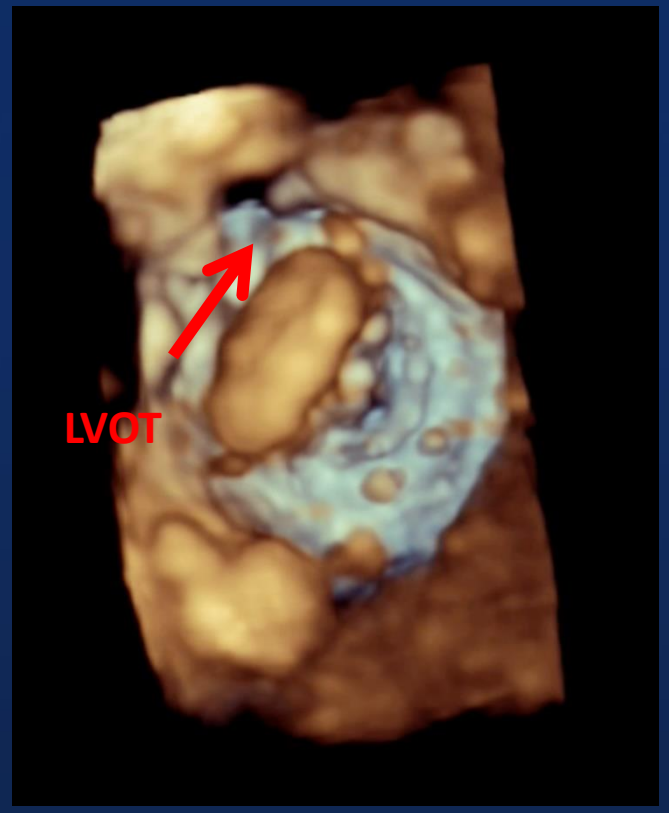
## Neo-LVOT

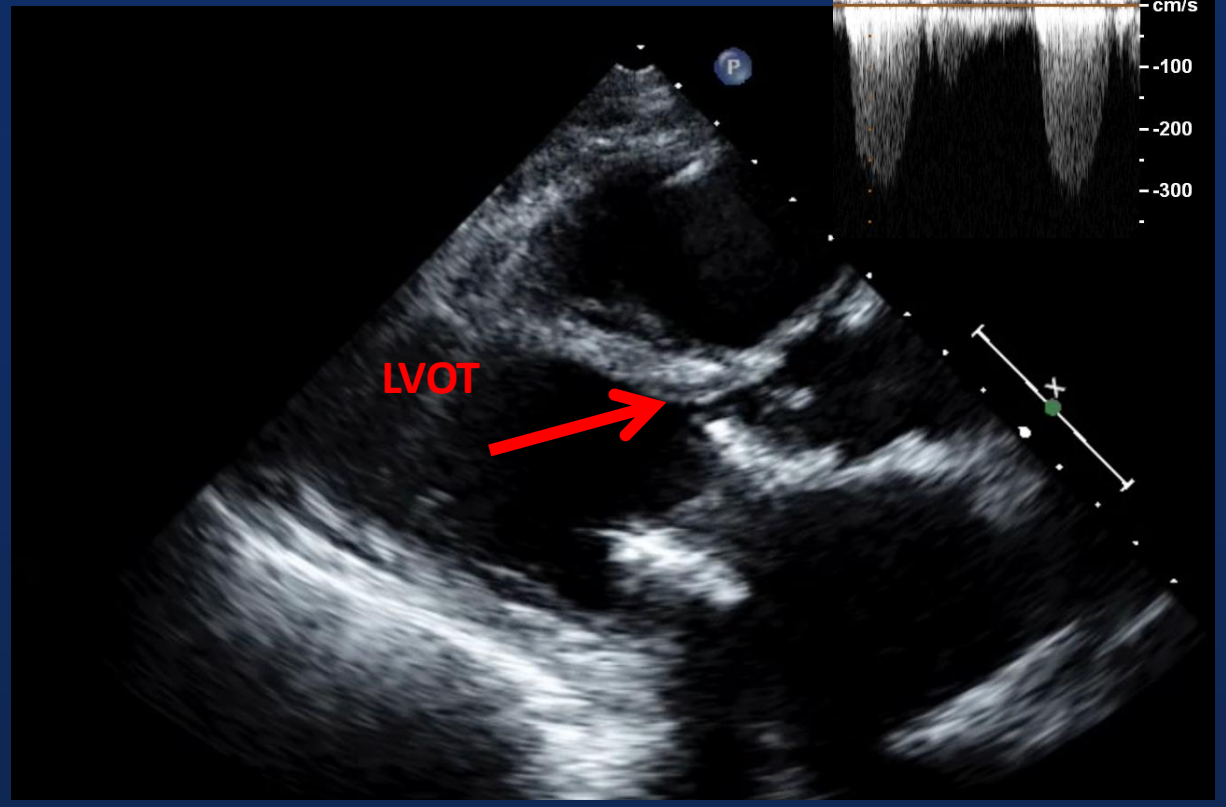



Blanke P. JACC CV imaging 2016.

# High risk for LVOT obstruction

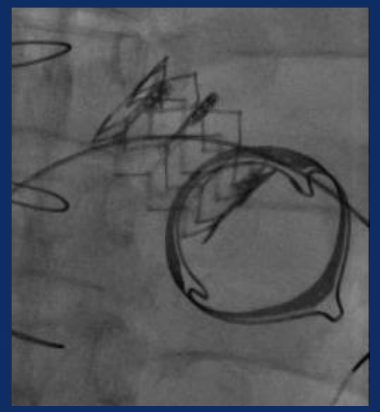
- 3.7% in the studied population.
- More common after Valve-in-Ring (8% vs. 2.6% in Valve-in-Valve , p=0.03).

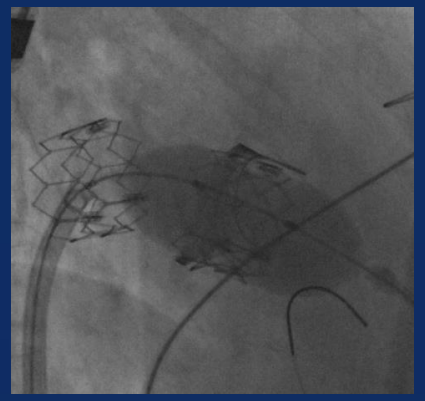
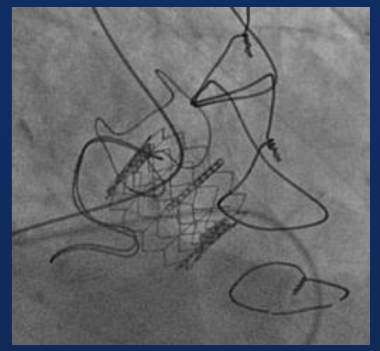
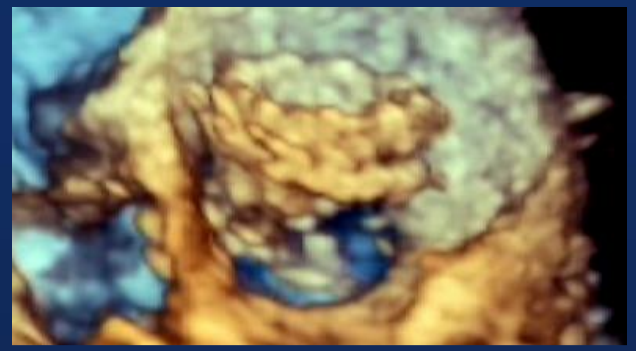
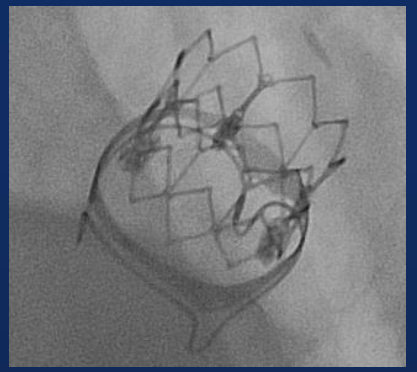



Ran Kornowski, TVT 2018

# Mal-positioning

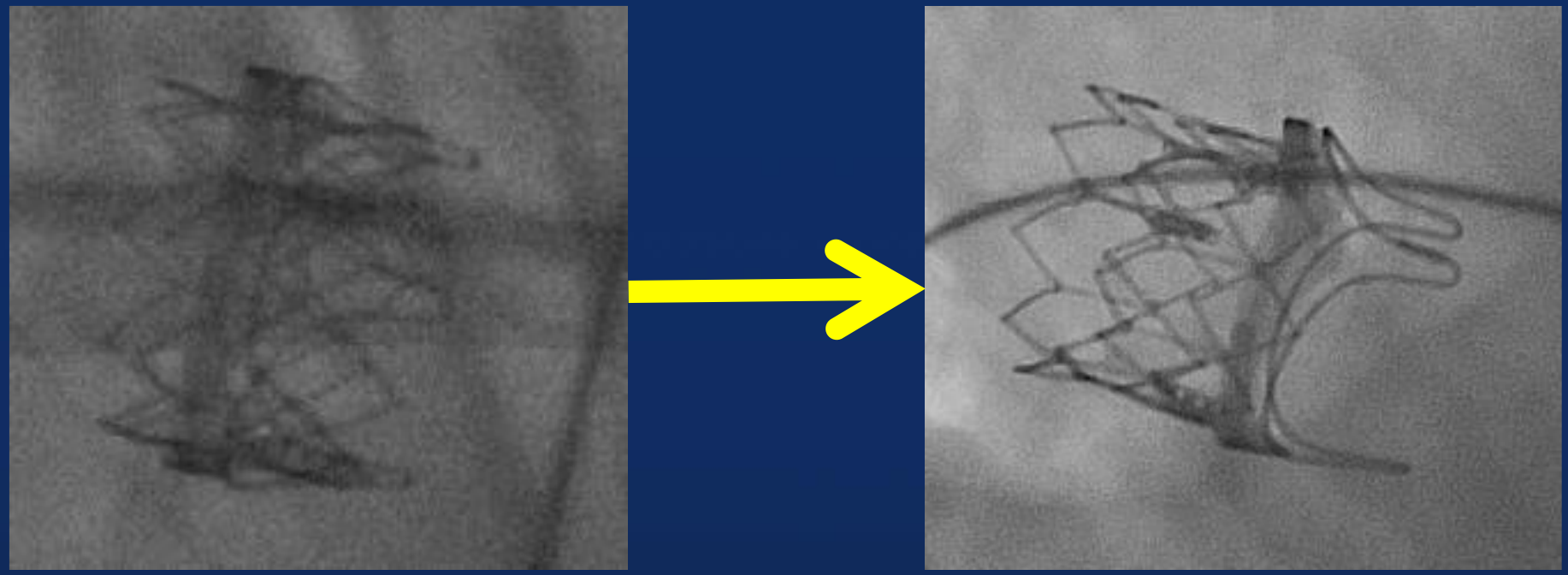


- 29 mal-positioning events (6.6%).
- 20 Implantation of another transcatheter device (4.6%).

Ran Kornowski, TVT 2018

# Delayed Mal-positioning



Mitral Valve-in-Valve

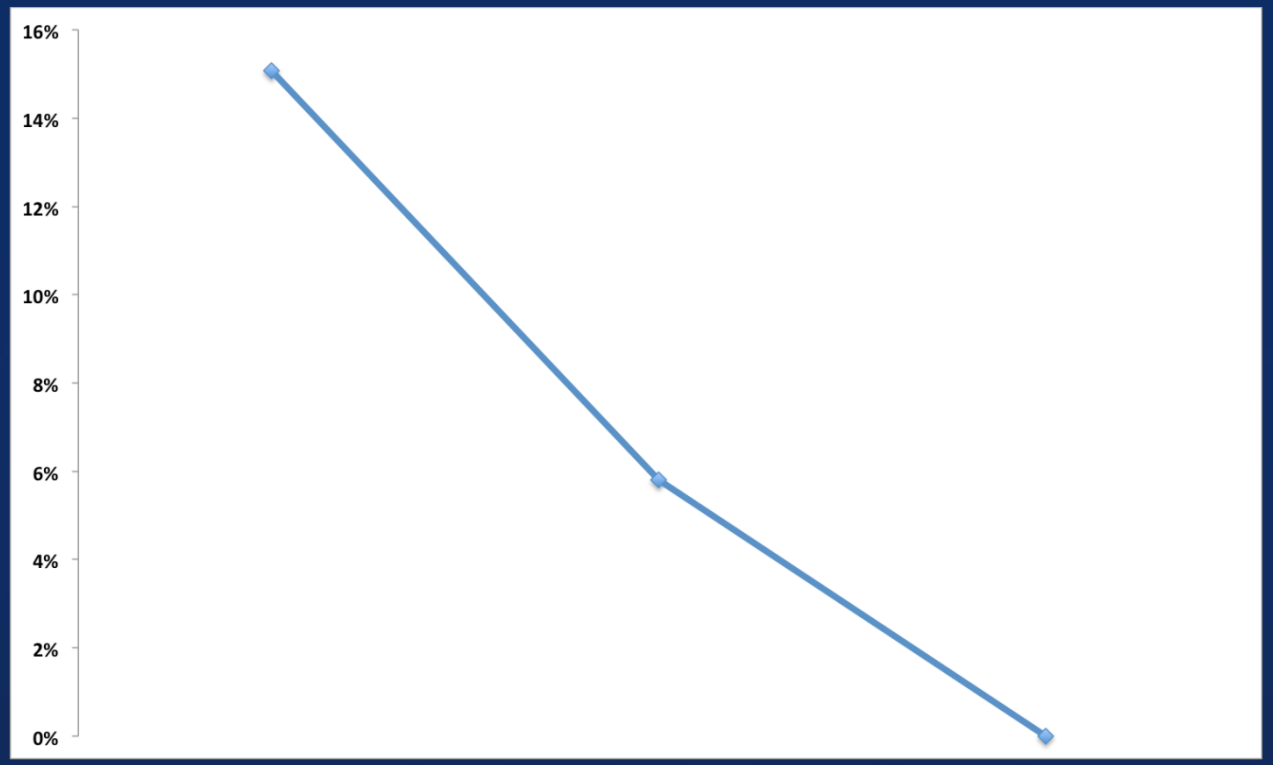
After 2 months

**Delayed malpositioning (>1 week) in 1.1%.**

Ran Kornowski, TVT 2018

# Residual stenosis

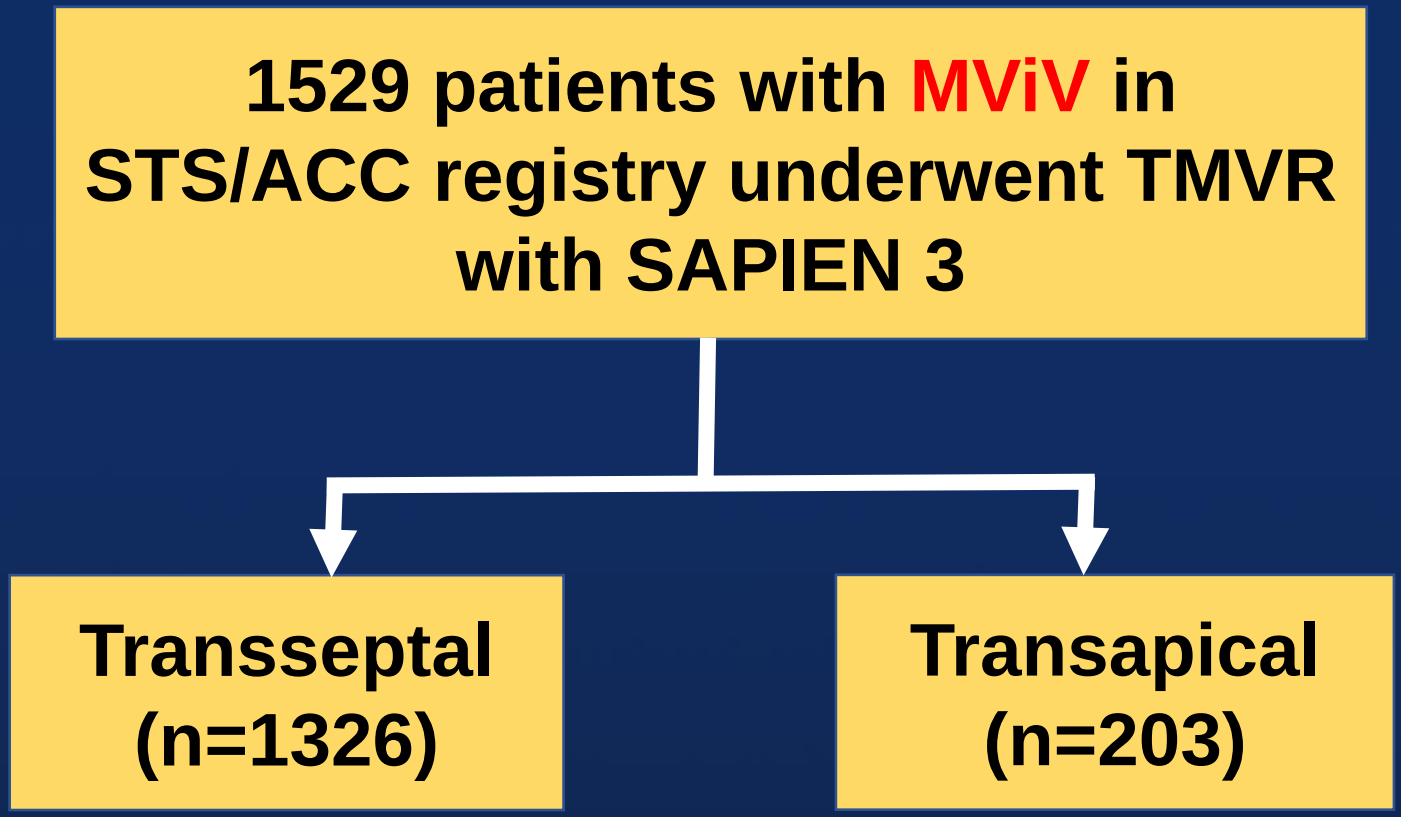
Elevated post procedural gradients (mean>=10mmHg)




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

Ran Kornowski, TVT 2018

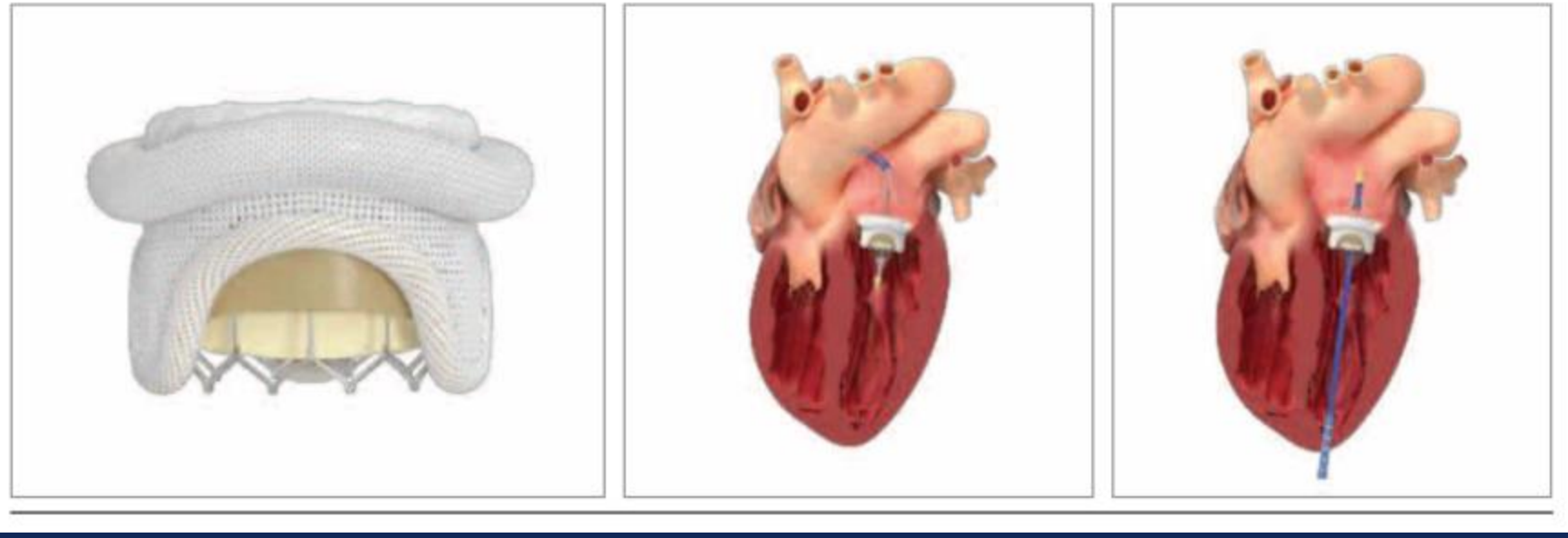
# One-Year Outcomes of Mitral VIV using SAPIEN 3




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






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

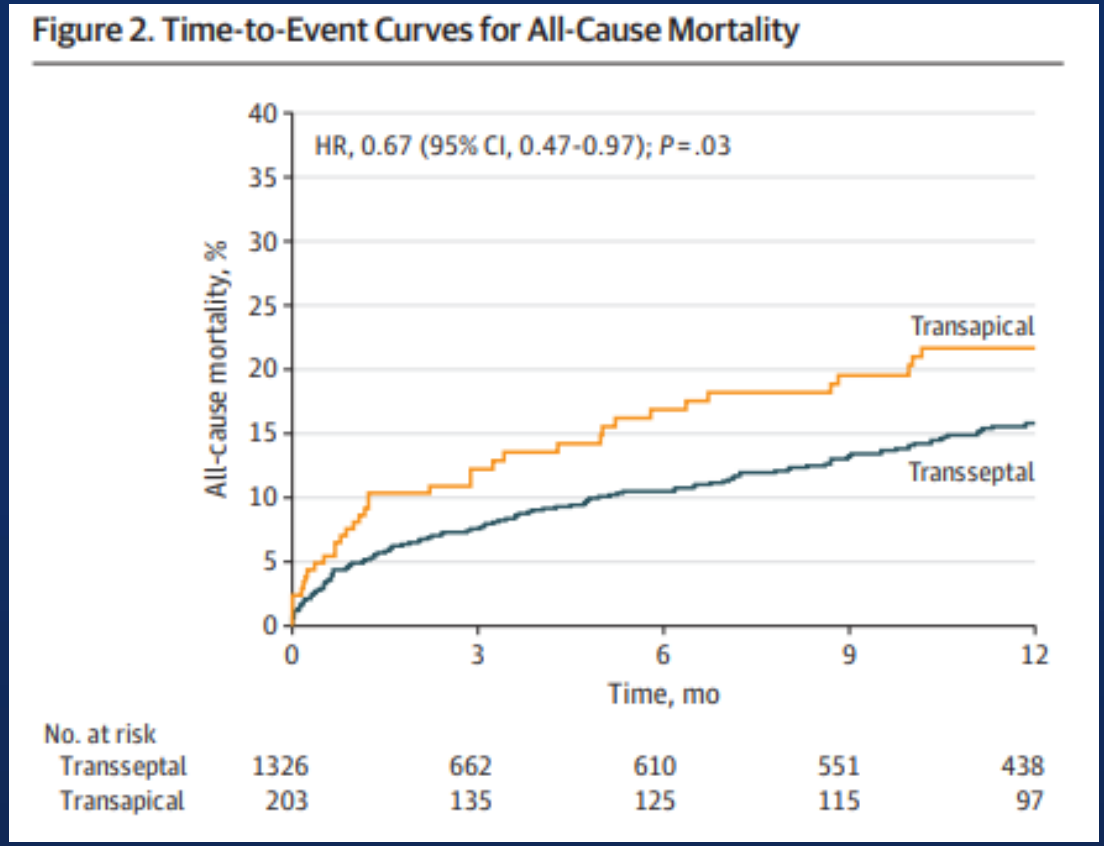
**Median follow up : 492 days**

**Transcatheter heart valves in failed bioprosthetic surgical valves (n =1079)**

- **Mitral valve in valve (n=857)**
- **Mitral valve in ring (n=222)**

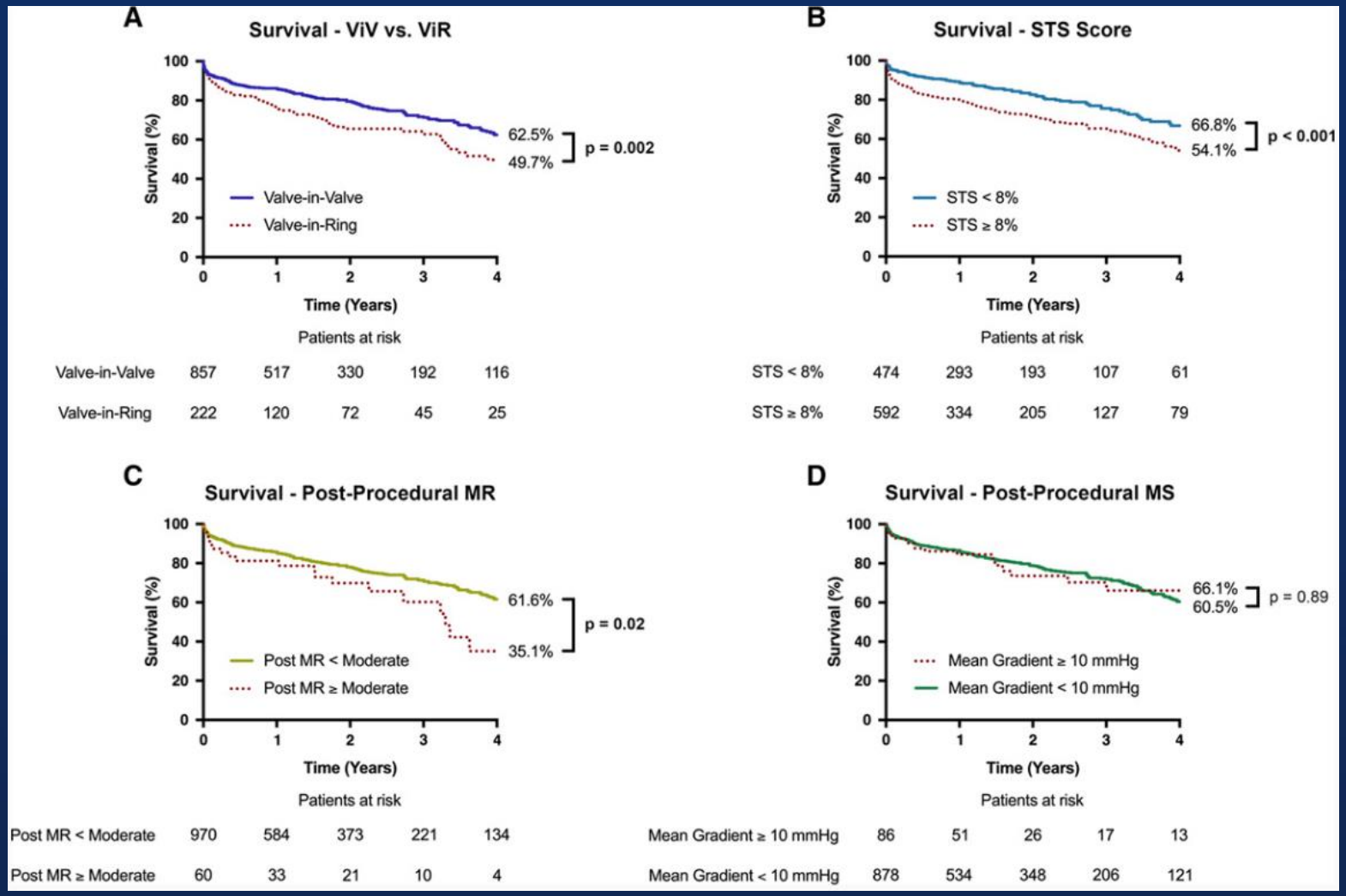
Matheus Simonato, 2021 circulation

# One-Year Outcomes of Mitral VIV using SAPIEN 3



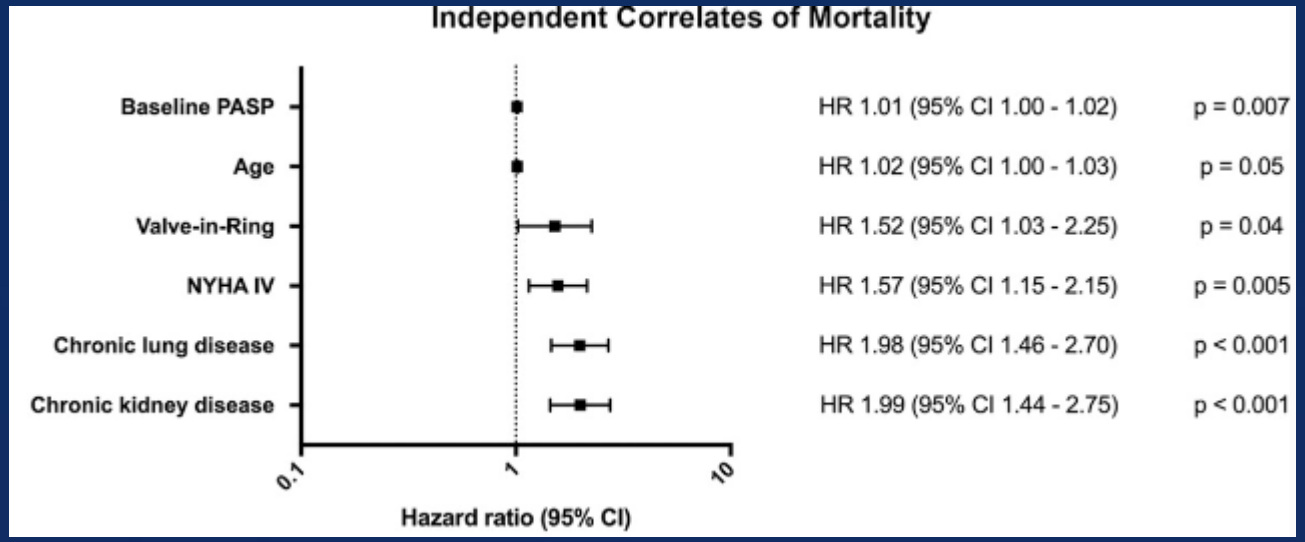

Brian Whisenant, 2020 JAMA

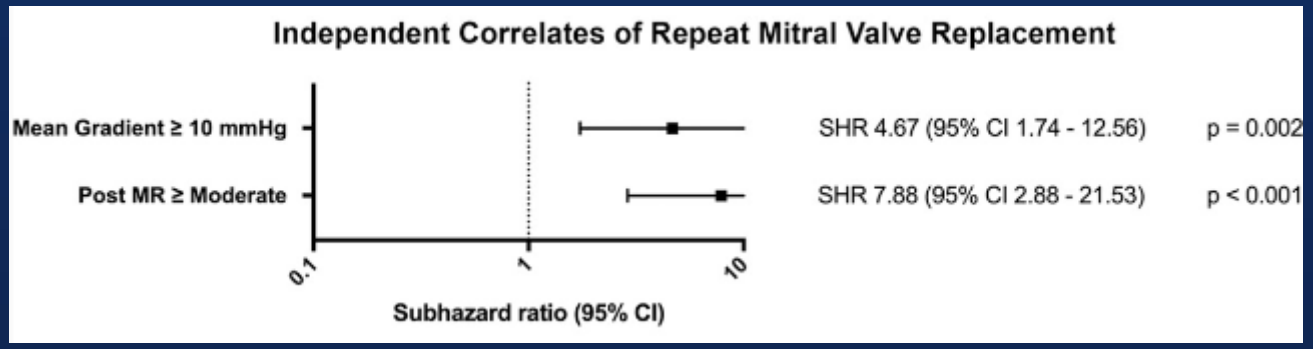
# Comprehensive midterm evaluation of VIVID Registry




Matheus Simonato, 2021 circulation

# Comprehensive midterm evaluation of VIVID Registry

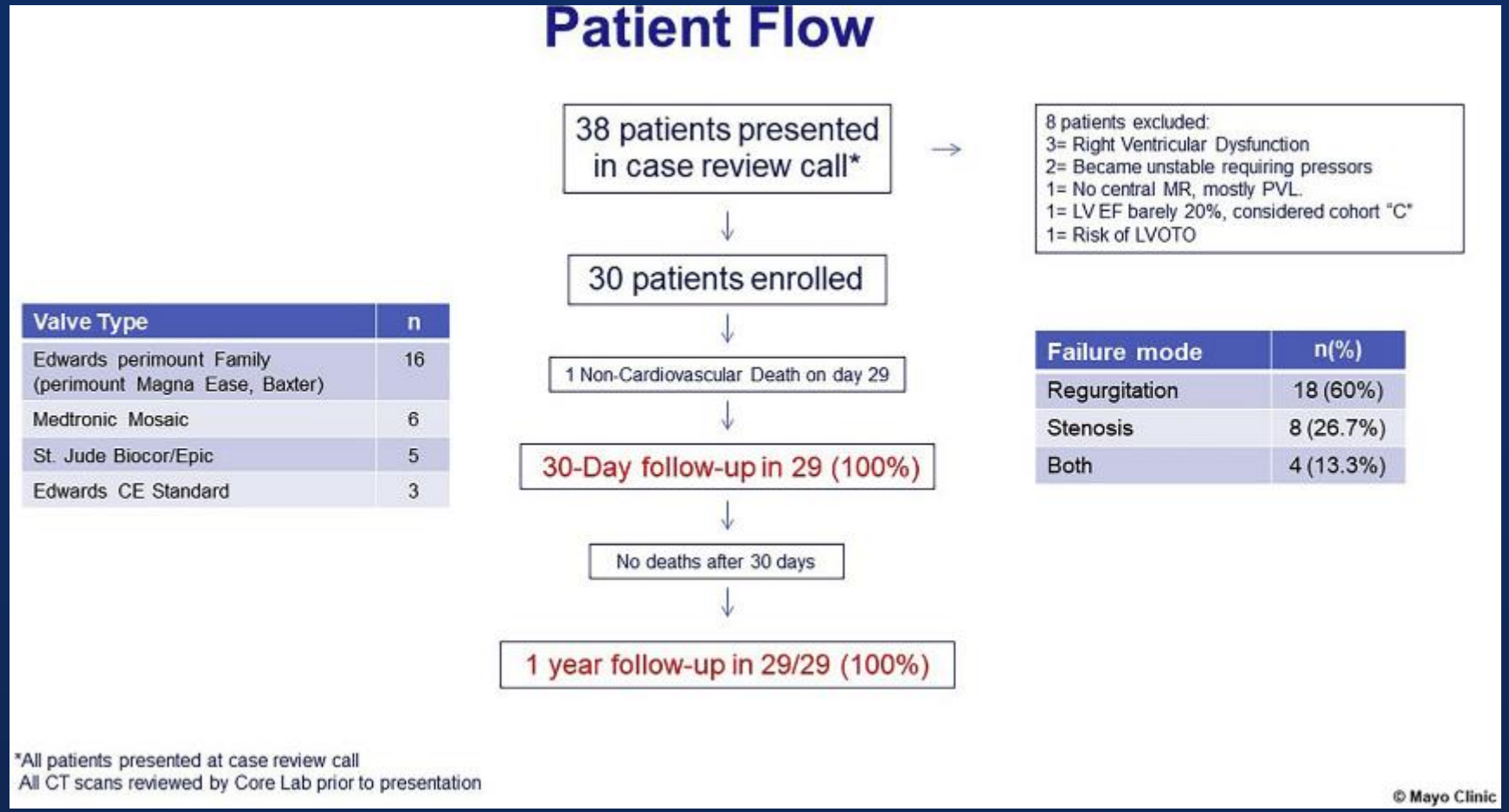




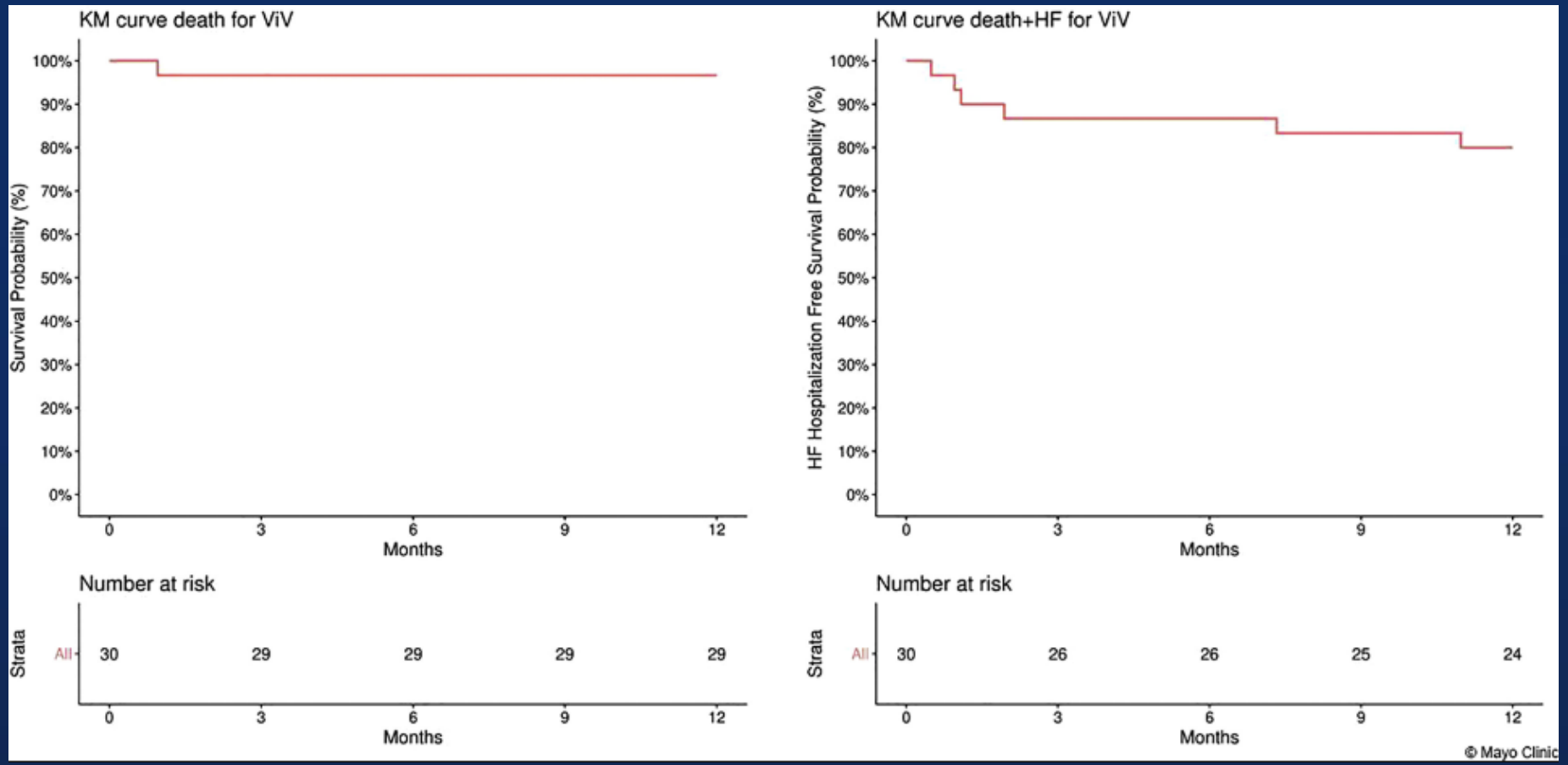

Matheus Simonato, 2021 circulation

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



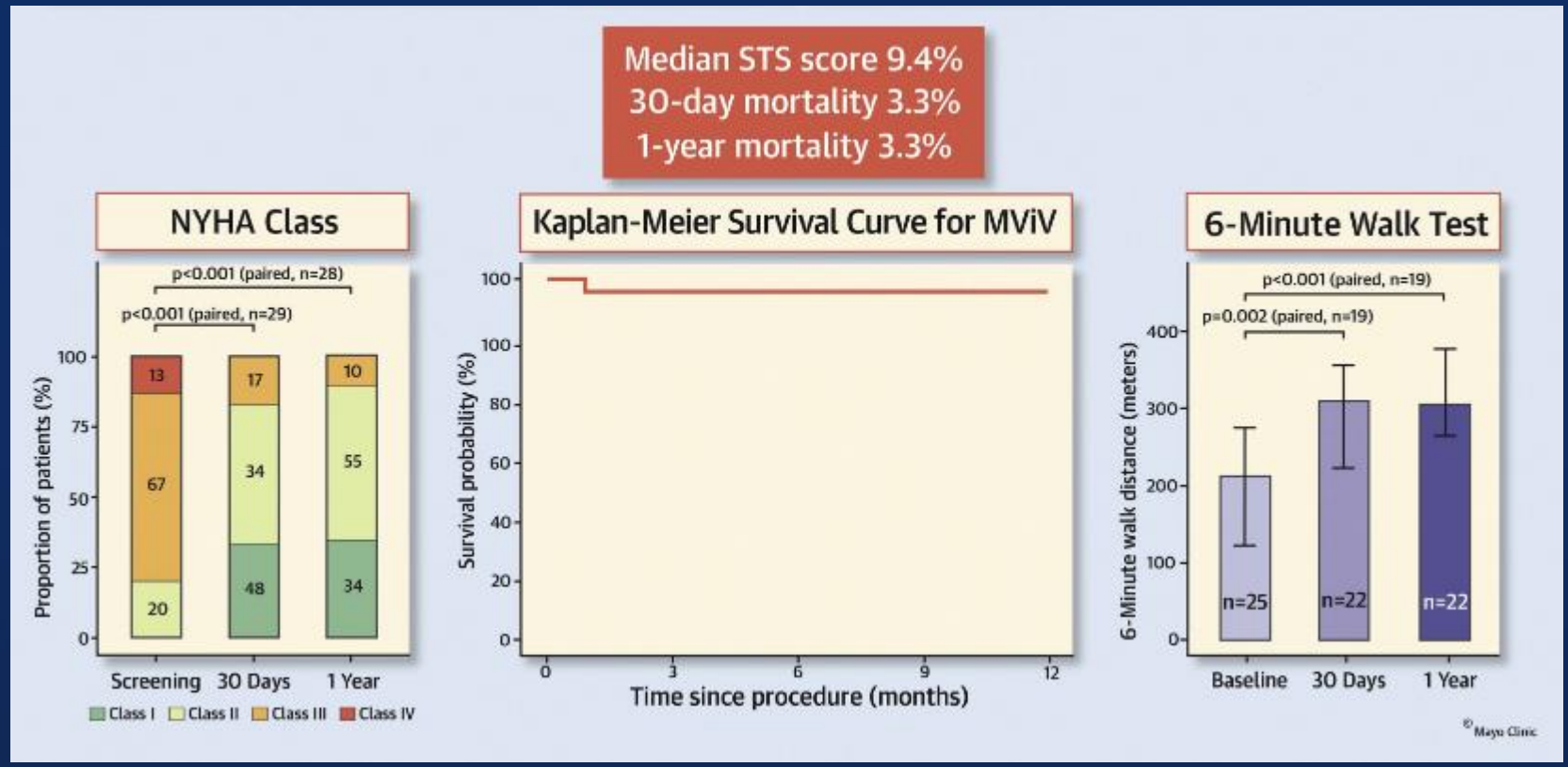

Mayra Guerrero, 2021 JACC
Prospective Evaluation of Transseptal TMVR for Failed Surgical Bioprostheses

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




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

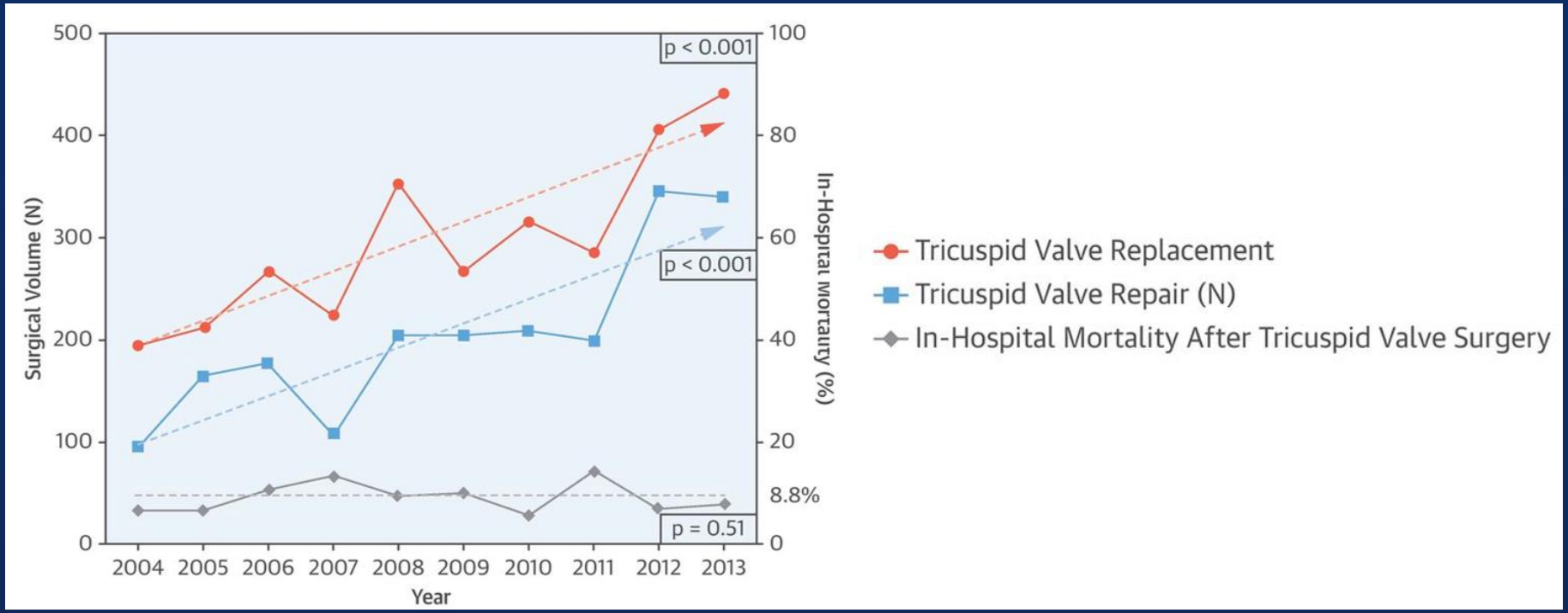
# MITRAL trial Valve-in-Valve Arm 1-Year Outcomes




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

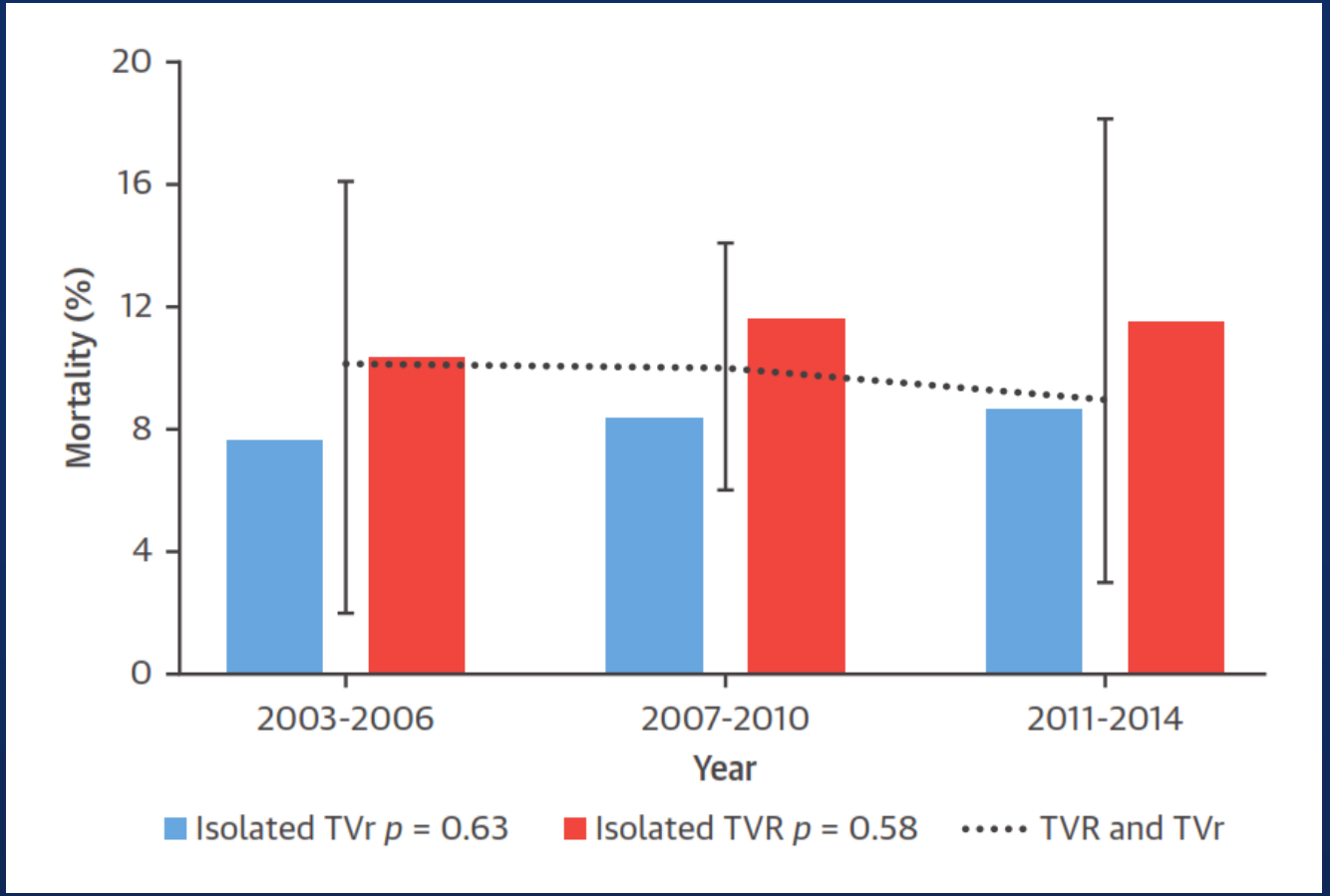
# ViV: Tricuspid Valve

# National Trends and Outcomes in Isolated Tricuspid Valve Surgery

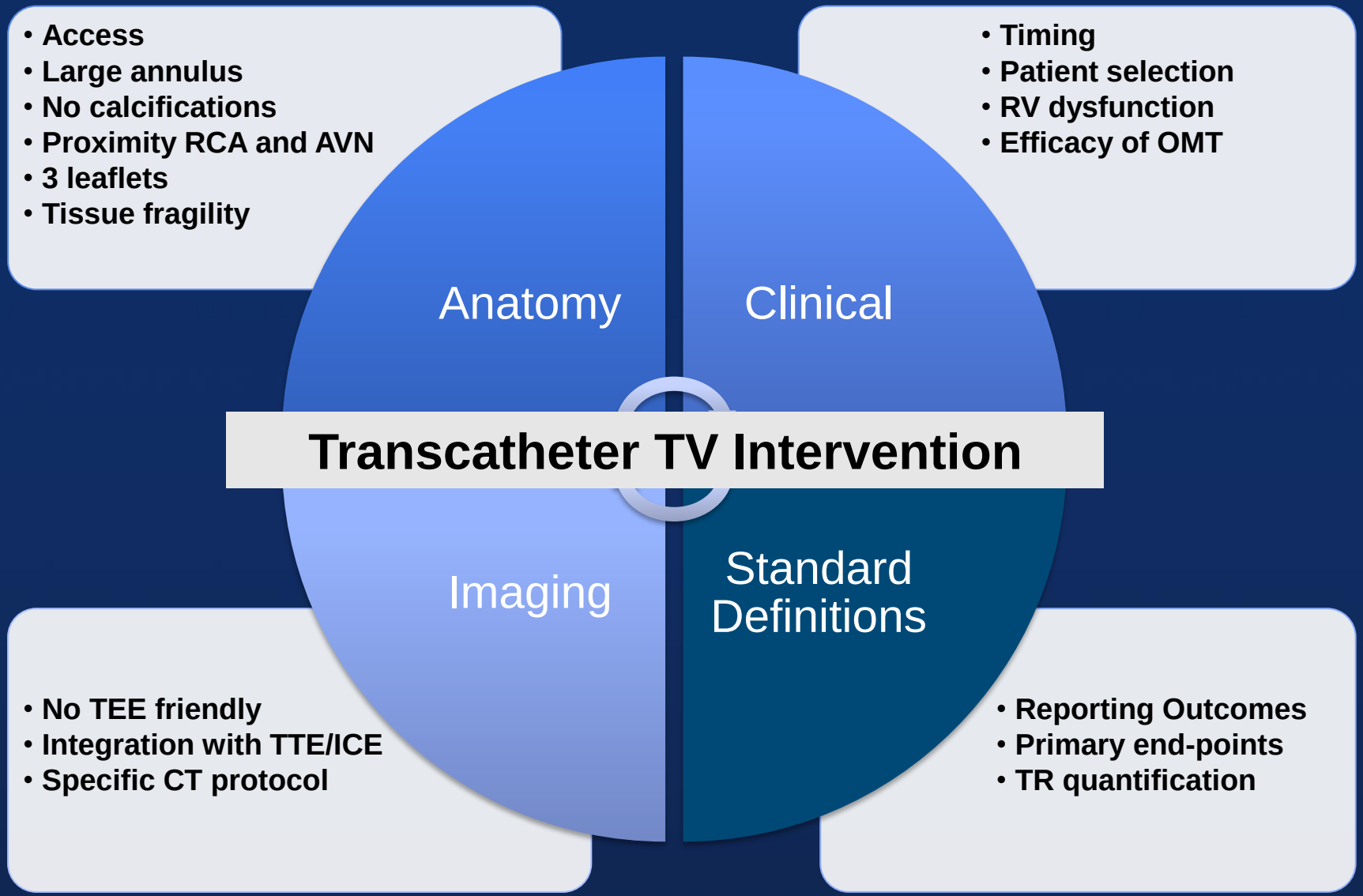



Zack, C.J. et al. J Am Coll Cardiol. 2017

# Surgical Mortality – Isolated TVR/TVr




Alqahtani F, et al. J Am Heart Assoc 2017

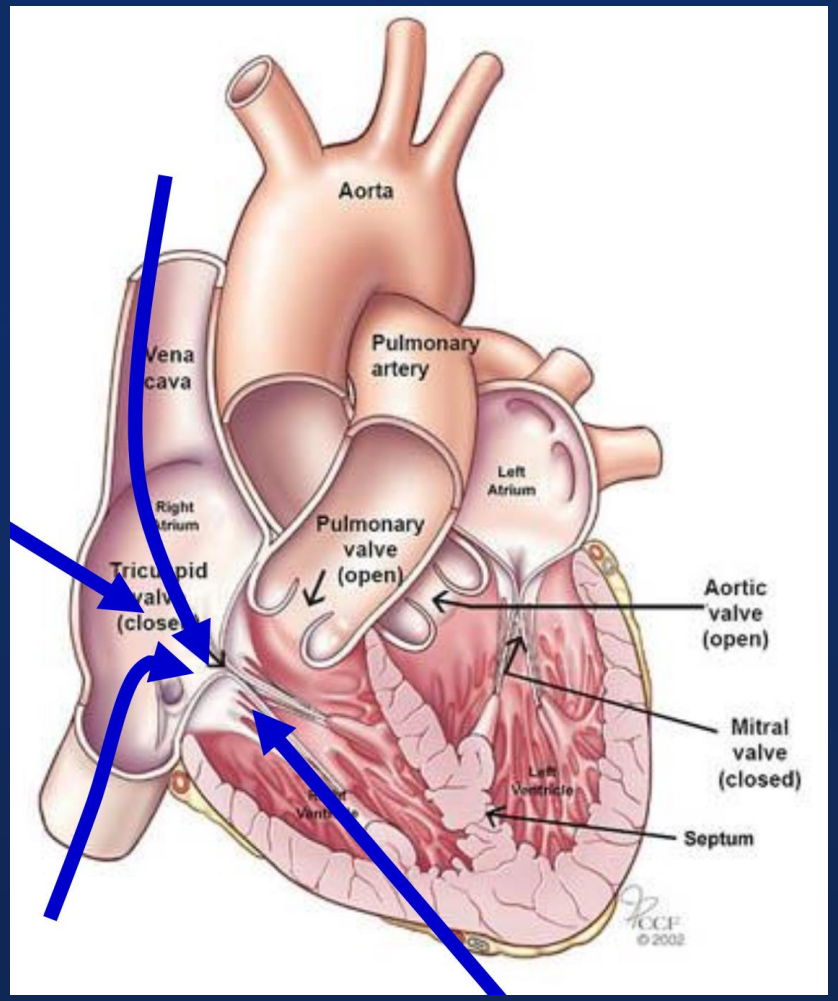

• Access
• Large annulus
• No calcifications
• Proximity RCA and AVN
• 3 leaflets
• Tissue fragility
• Timing
• Patient selection
• RV dysfunction
• Efficacy of OMT
Anatomy
Clinical
Transcatheter TV Intervention
Imaging
Standard Definitions
• No TEE friendly
• Integration with TTE/ICE
• Specific CT protocol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



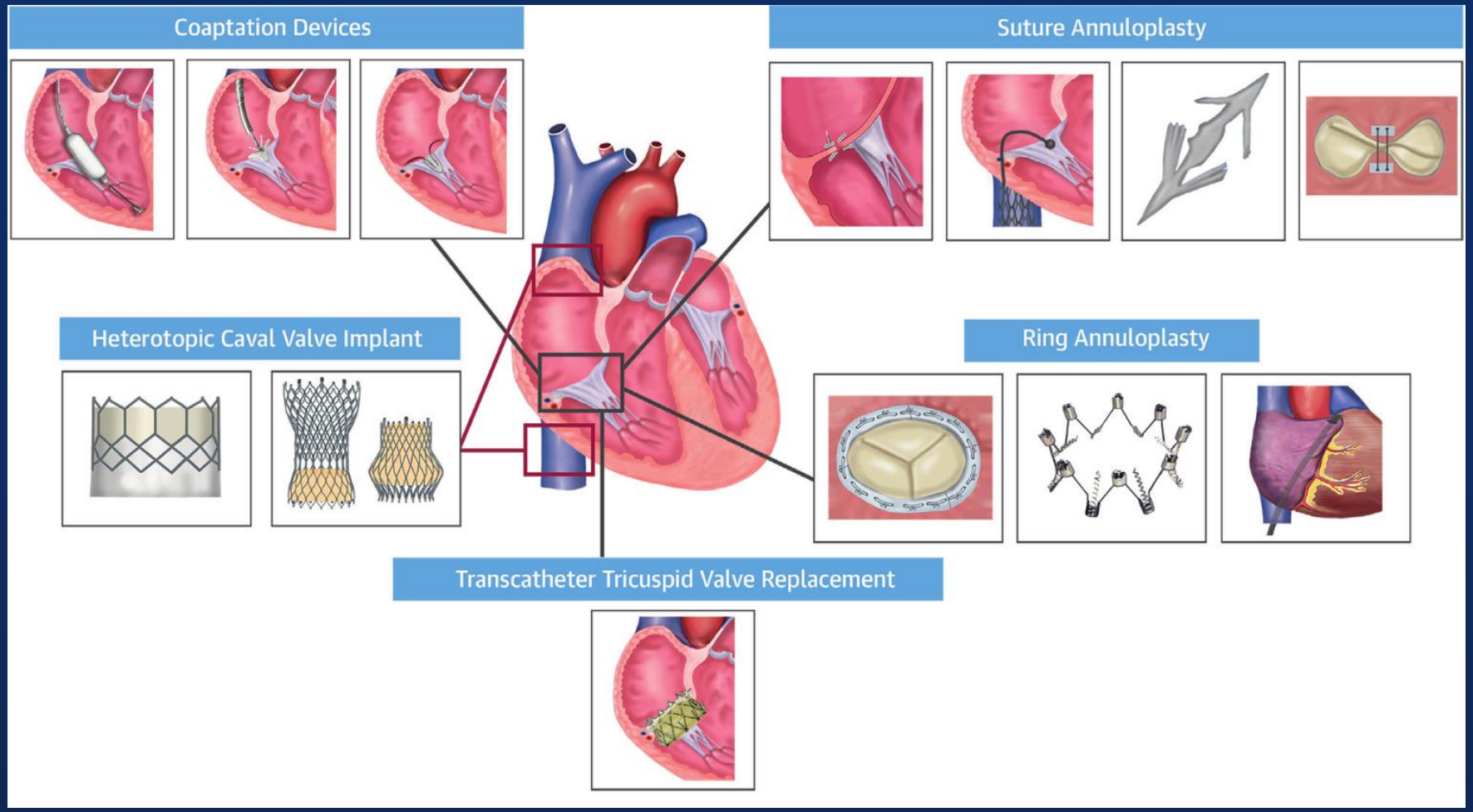

**Approaches**

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

**Anatomic Target**

1. Leaflet
2. Annulus
3. IVC

# Transcatheter Tricuspid Landscape

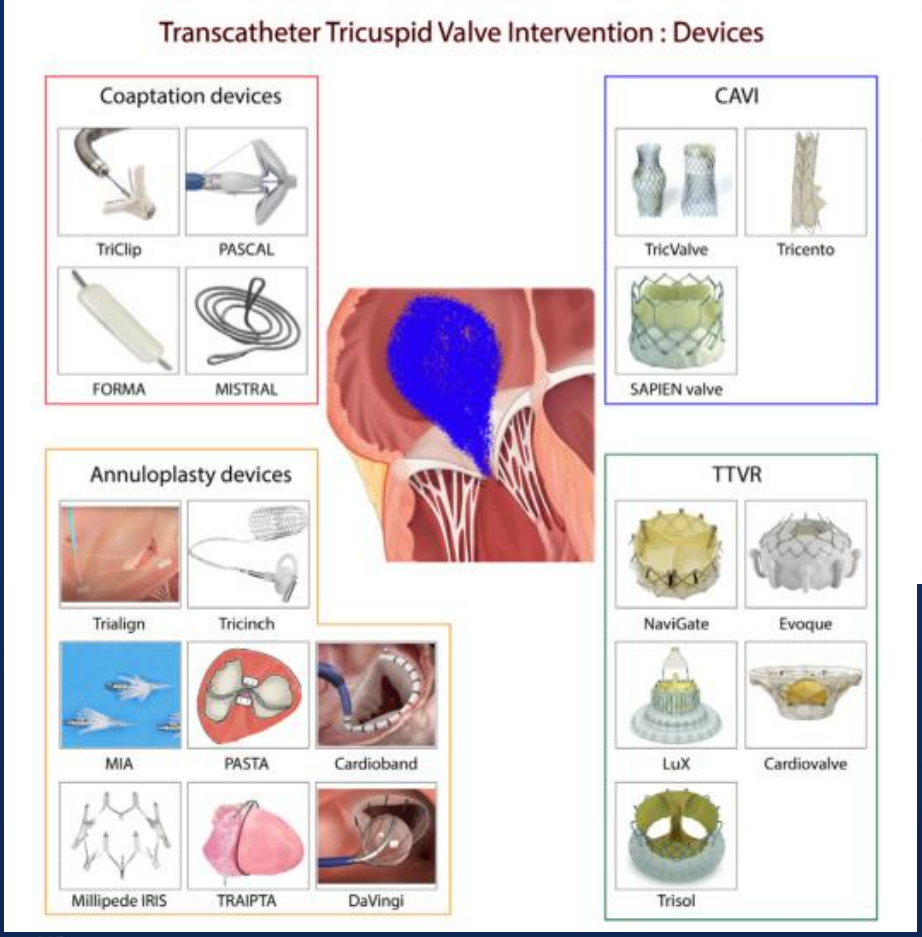







Asmarats et al. J Am Coll Cardiol. 2018;71(25):2935-56

# Transcatheter Tricuspid valve : Devices

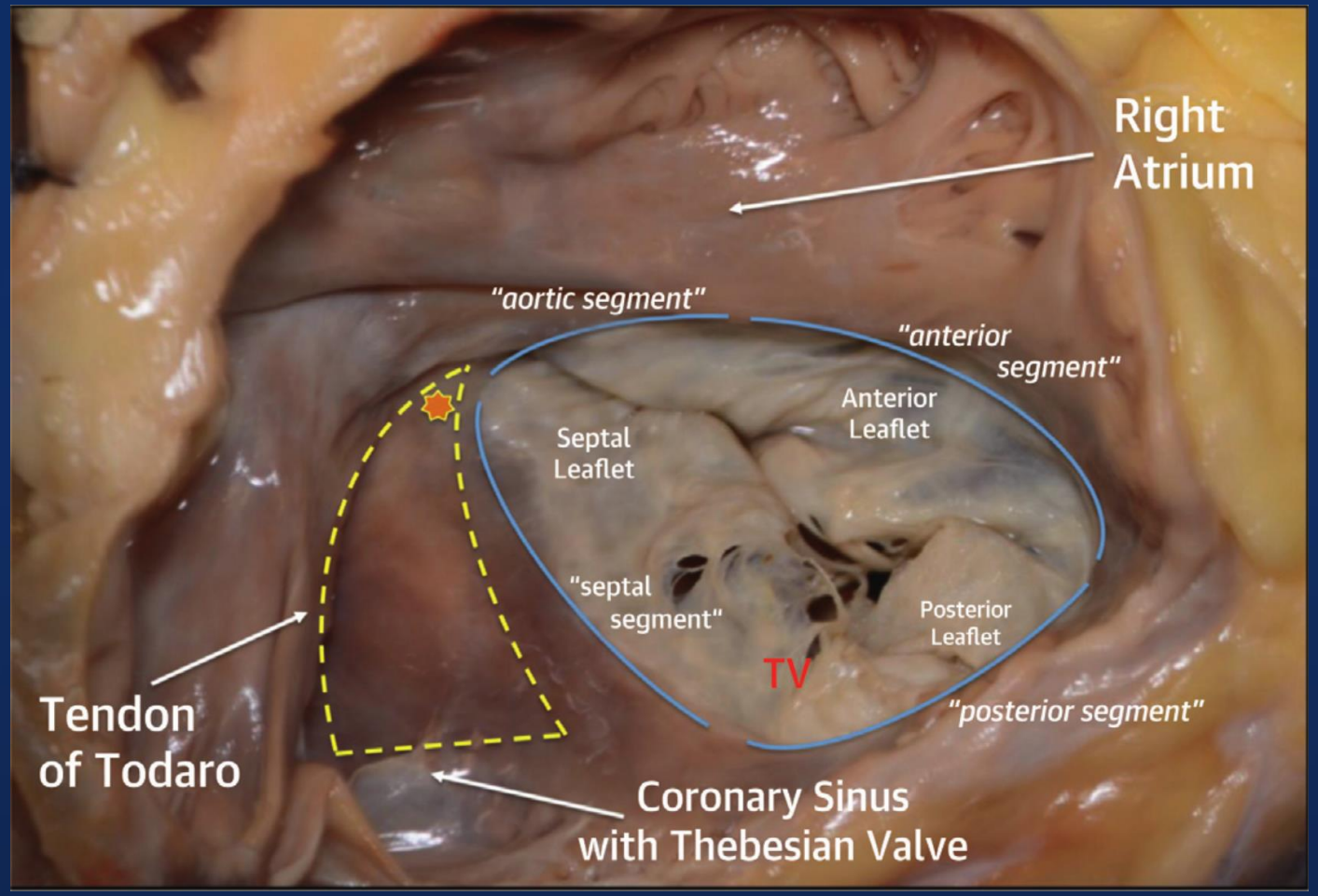



| Device | Study | *Baseline characteristics* Age, years | NYHA III/IV | CIED | Functional TR | *Procedural outcomes* Procedural success | Conversion to surgery | Residual TR ≥ grade 3 | 30-day mortality |
|---|---|---|---|---|---|---|---|---|---|
| TriClip | TriValve ($n = 249$)[46] | 77 ± 9 | 238 (96) | 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<br>Tricuspid valve tethering associated with perimembranous VSD and VSA<br>Other (giant right atrium) |
| | Acquired disease | Carcinoid<br>Degenerative (myxomatous)<br>Endocarditis<br>Endomyocardial fibrosis<br>Iatrogenic (pacing leads, RV biopsy)<br>Rheumatic<br>Toxins<br>Trauma<br>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)<br>RV ischemia<br>RV volume overload |
| | Pulmonary Hypertension | Chronic lung disease<br>Left-to-right shunt<br>Pulmonary thromboembolism |
| | Right atrial abnormalities | Atrial fibrillation |
| Other | Post-operative | Recurrent TR post-surgical intervention |

# TTVI sytems selection

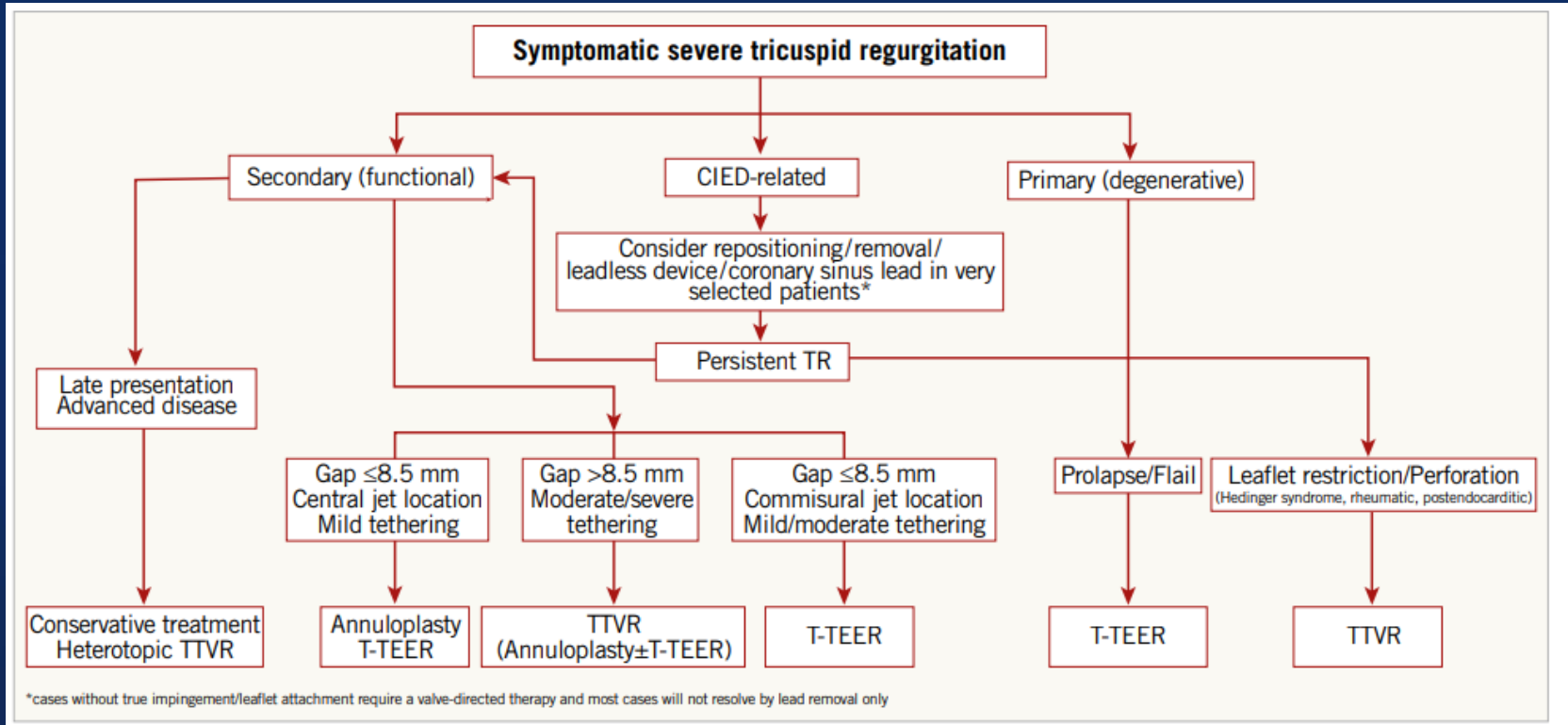



**Figure 6.** *Proposed algorithm for the selection of TTVI systems. CIED: cardiac implantable electronic device; T-TEER: tricuspid transcatheter edge-to-edge repair; TTVR: transcatheter tricuspid valve replacement*



EuroIntervention 2021;17:791-808

# Criteria for device selection

**Table 3. Anatomical criteria for device selection.**

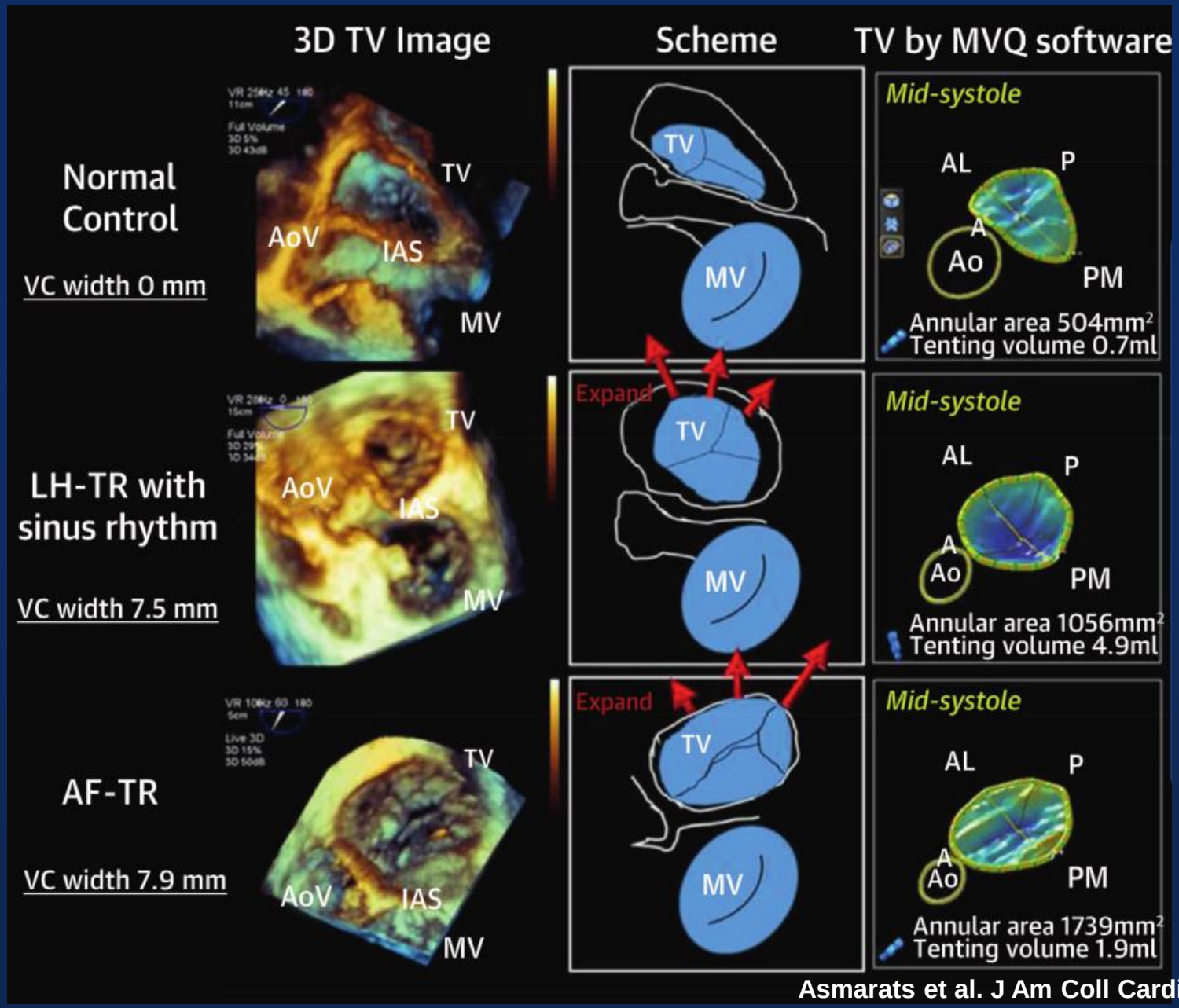
| Strategy | Favourable anatomy | Feasible anatomy | Unfavourable anatomy |
|---|---|---|---|
| Leaflet approximation | Small septolateral gap ≤7 mm[10]<br>Anteroseptal jet location<br>Confined prolapse or flail<br>Trileaflet morphology | Septolateral coaptation gap >7 but ≤8.5 mm[65]<br>Posteroseptal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



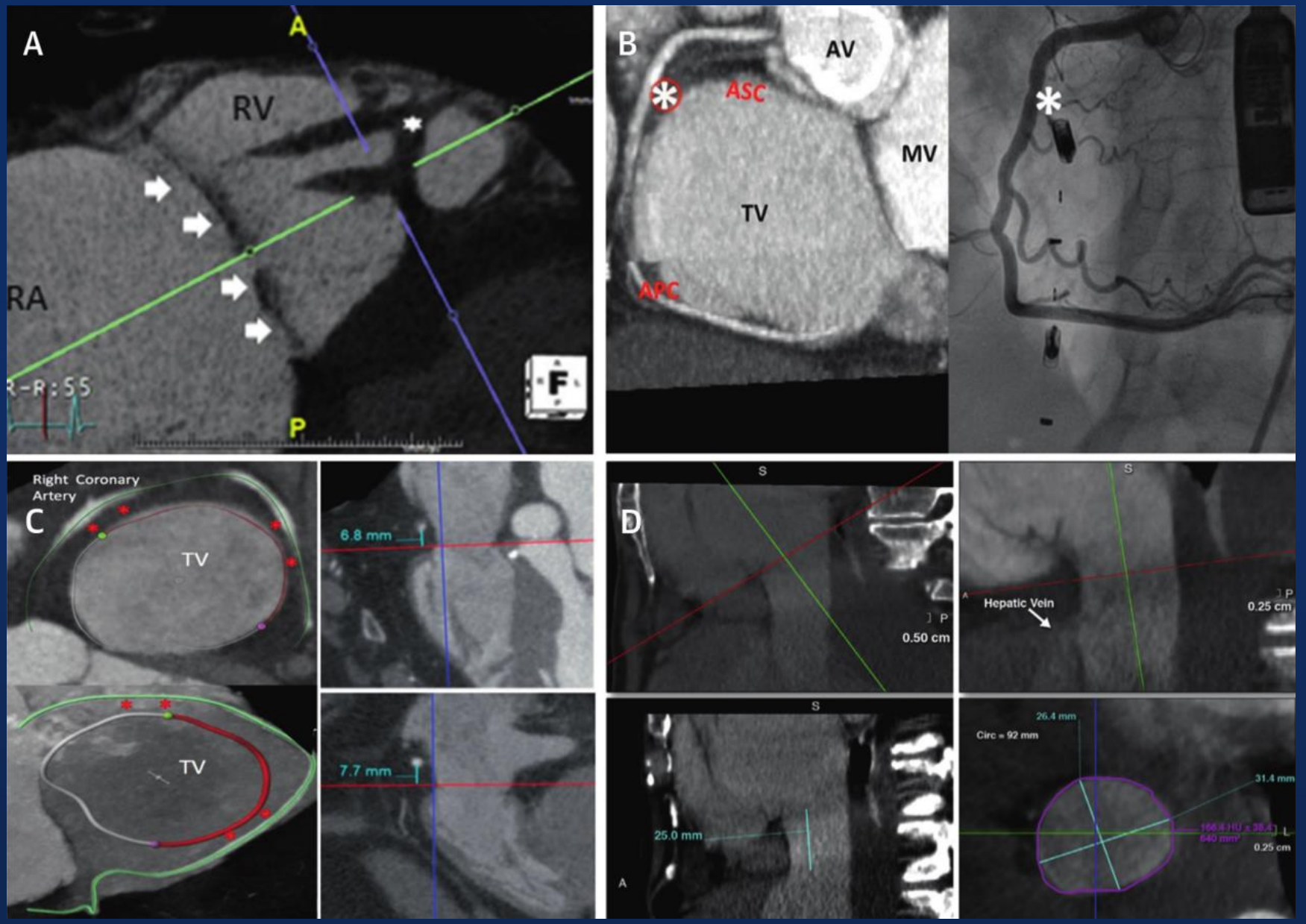
EuroIntervention 2021;17:791-808

# Pathoanatomy of Functional TR




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

# CT Pre-Procedural Workup





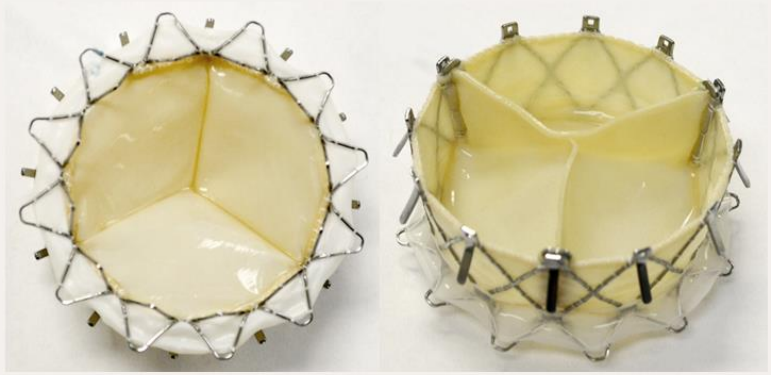



Asmarats et al. J Am Coll Cardiol. 2018;71(25):2935-56

# 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

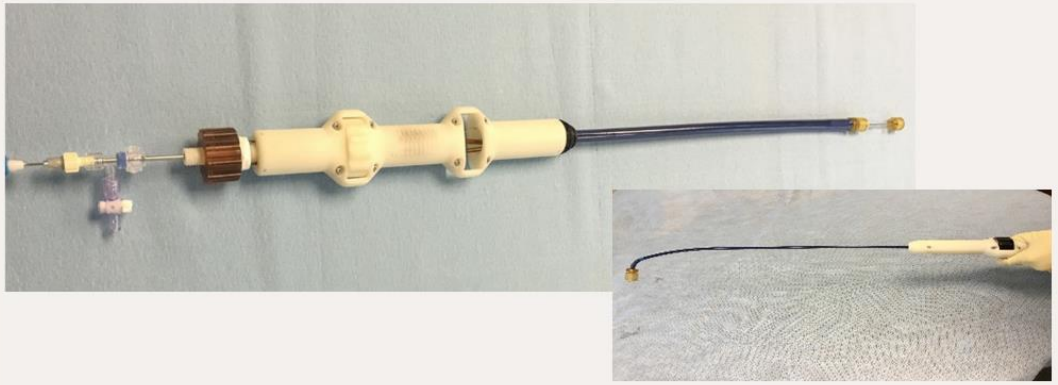
# Orthotopic TTVR
# NaviGate Tricuspid Valved Stent



## 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



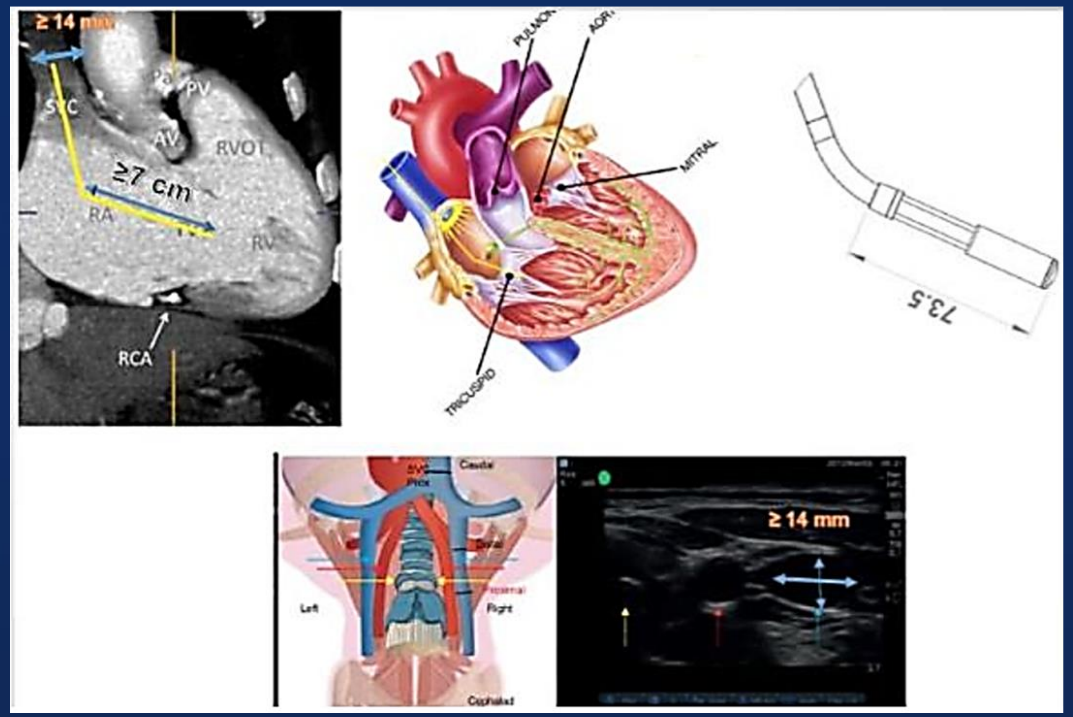
- Presently 35F at the distal capsule
- 24F catheter shaft
- Two degrees of motion at tip
- 80° Articulation
- Controlled Valve Release
- The delivery use the same valve configuration

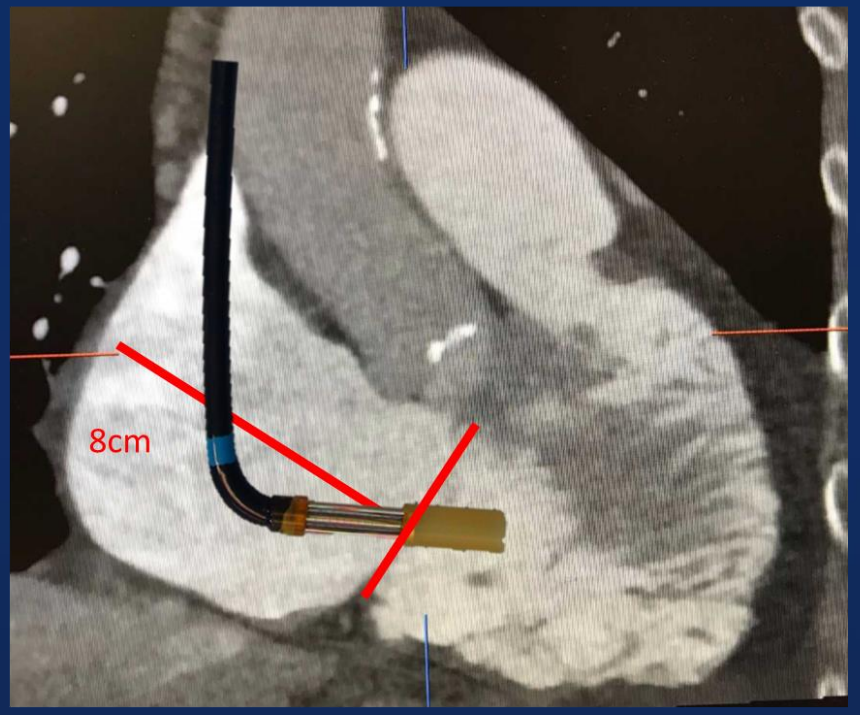




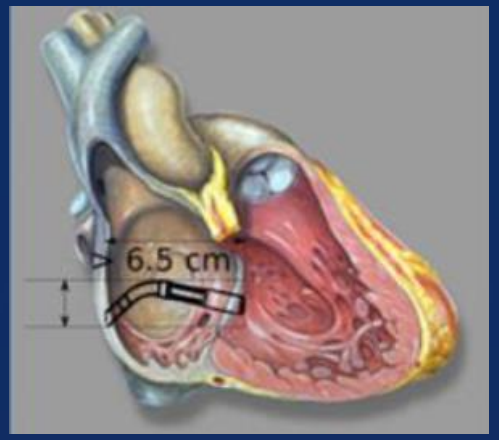
Asmarats et al. J Am Coll Cardiol. 2018;71(25):2935-56

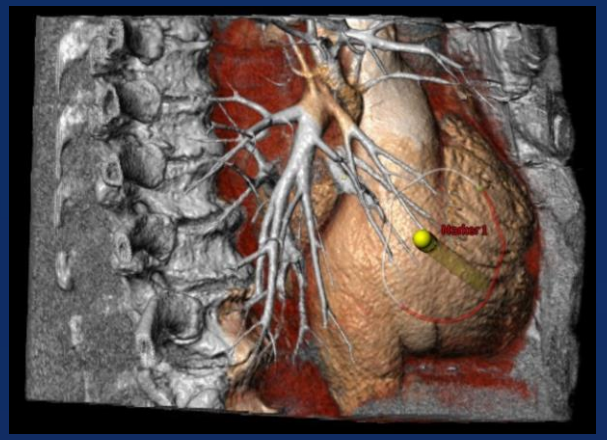
# Orthotopic TTVR
## Trans Jugular Requirements

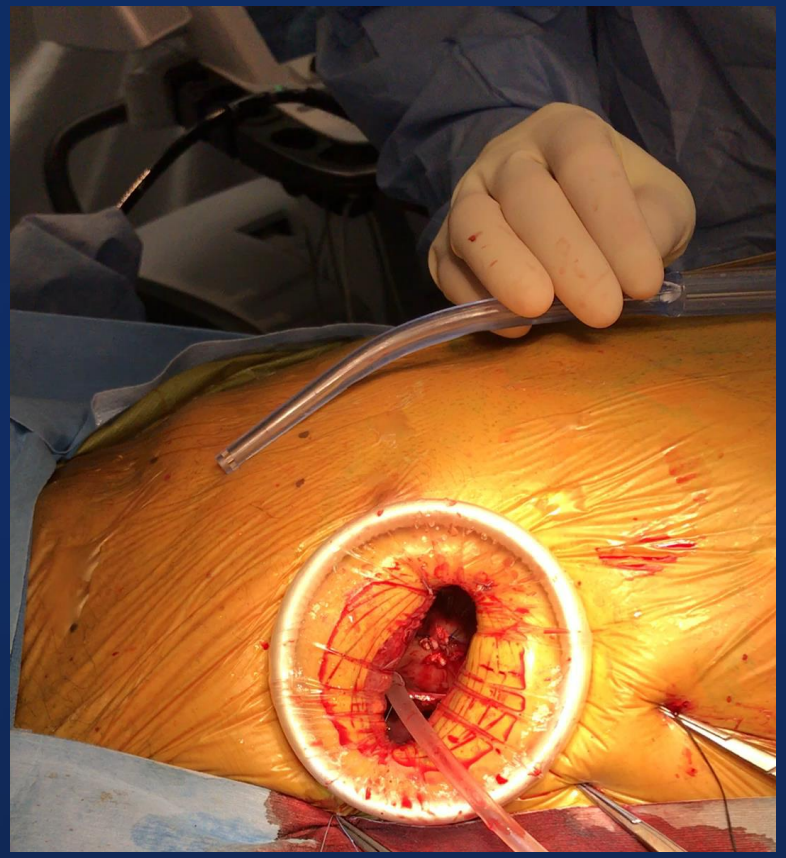


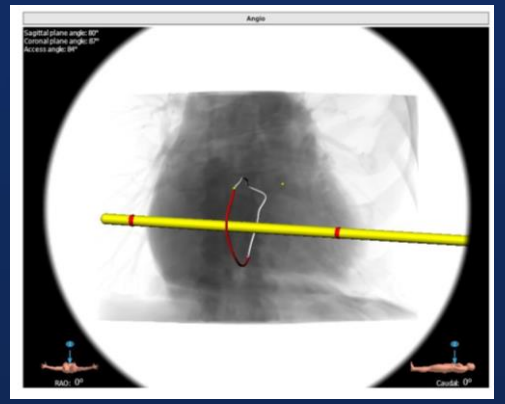



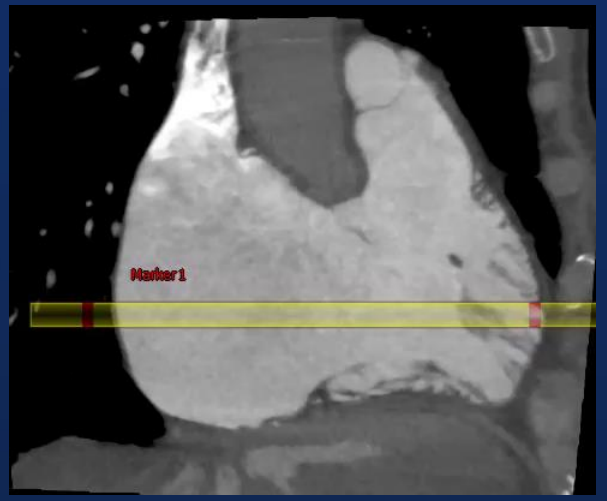
# Orthotopic TTVR
## Right Atrial Access



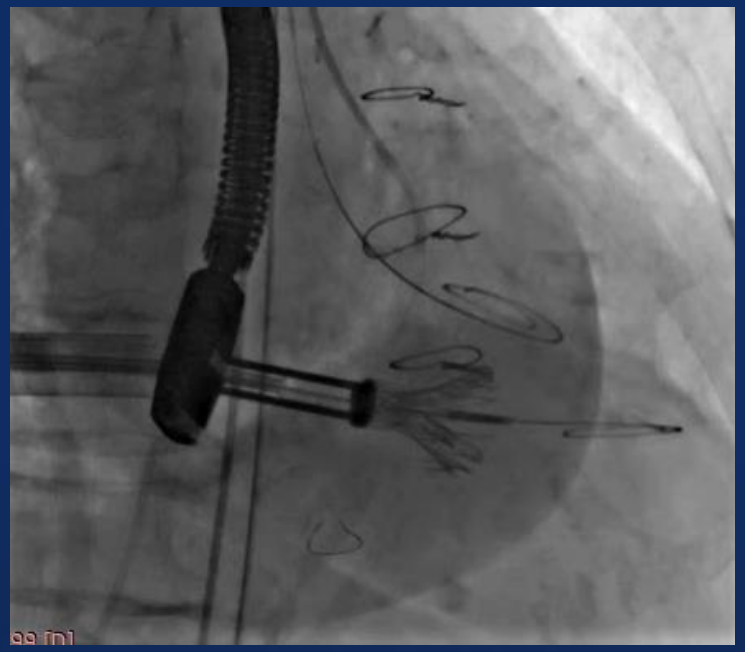



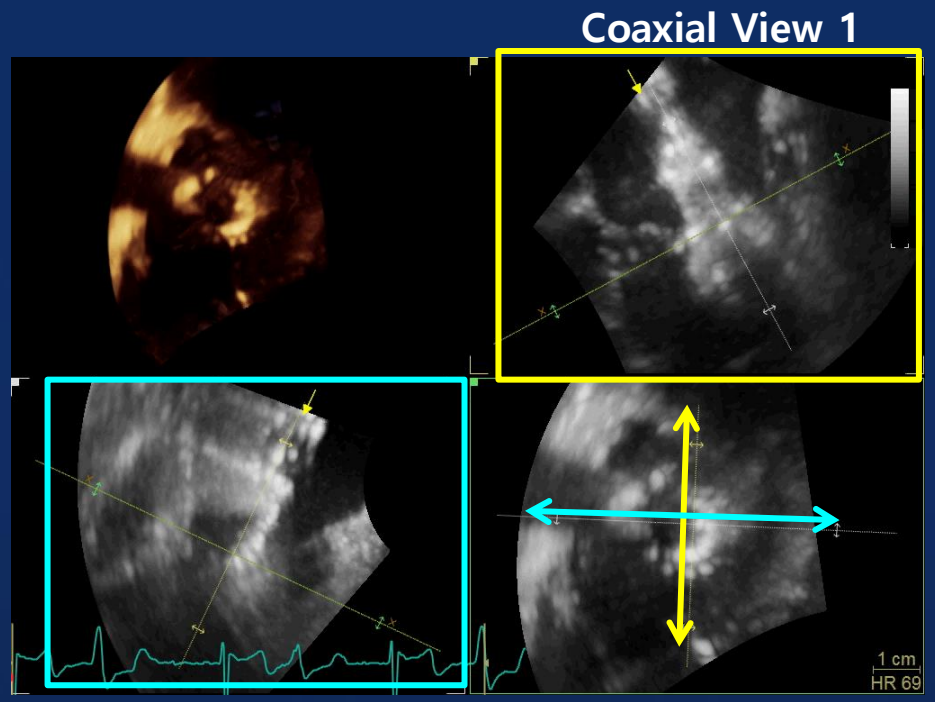




# Initial valve deployment with RCA injection



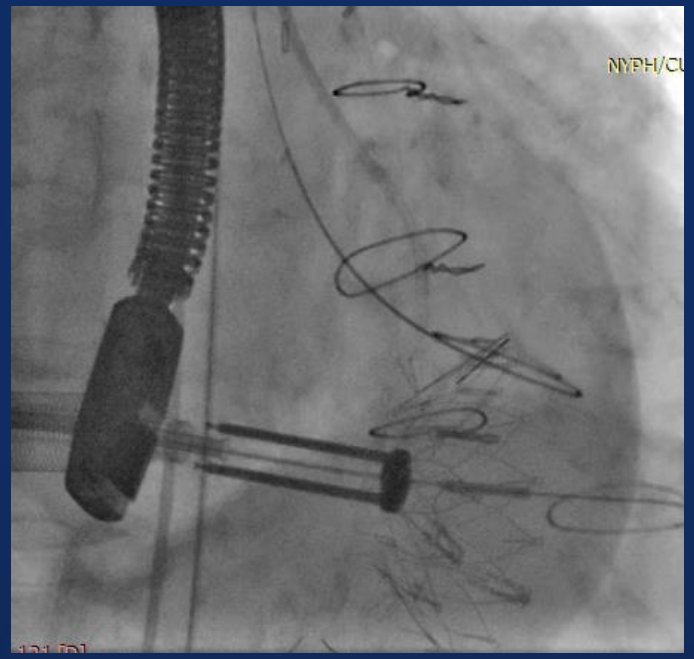
Retracting the capsule:
Exposing Ventricular Tines

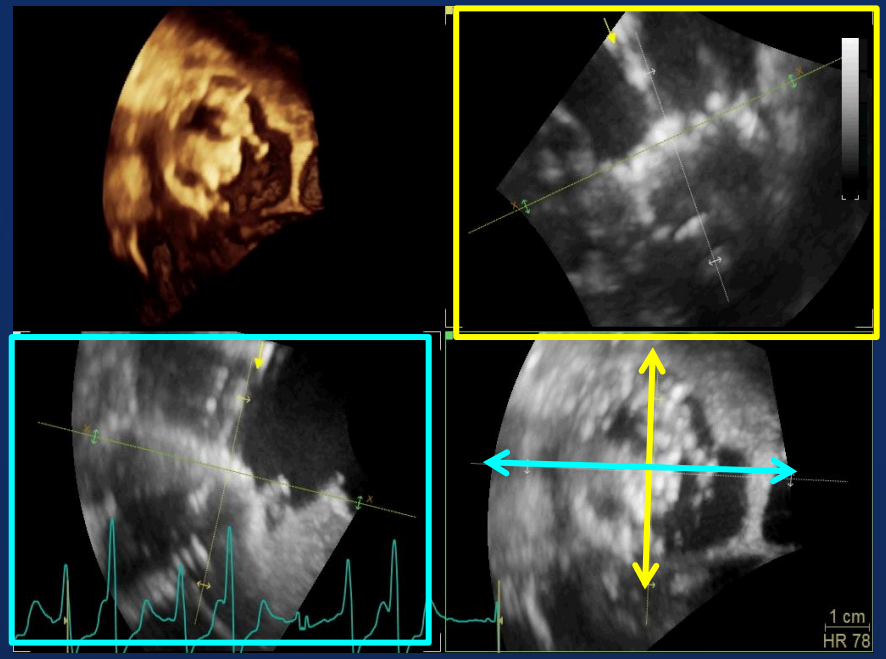



Coaxial View 2

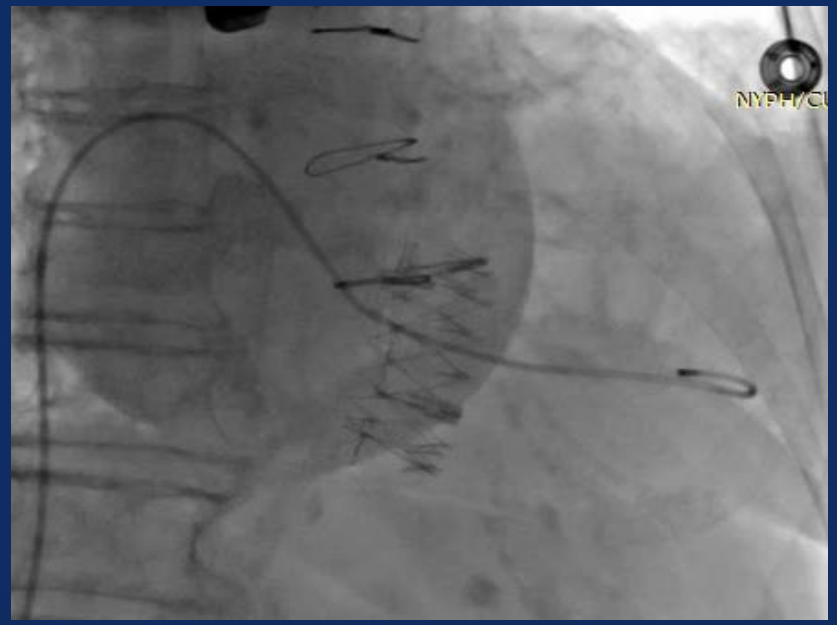
Short-axis View

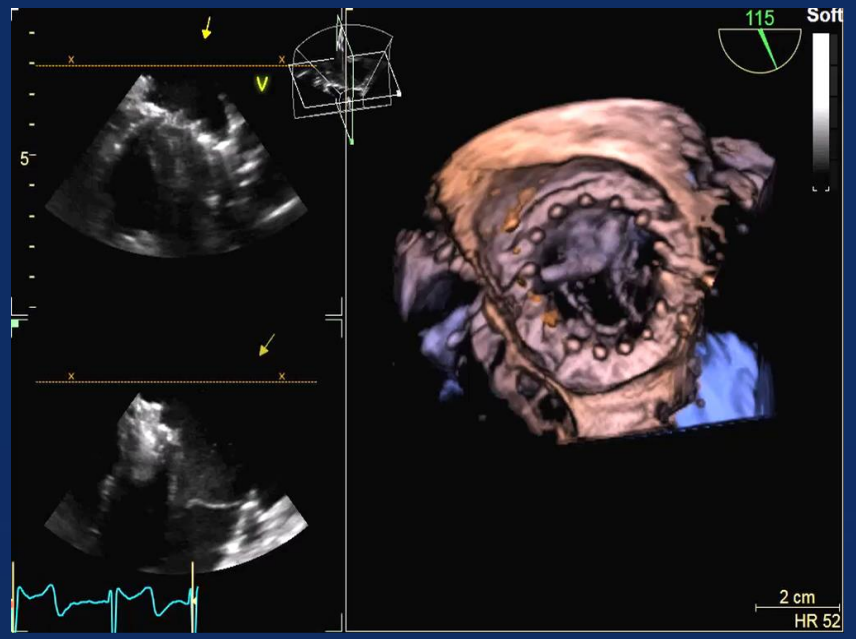
# Valve Release: Complete Deployment

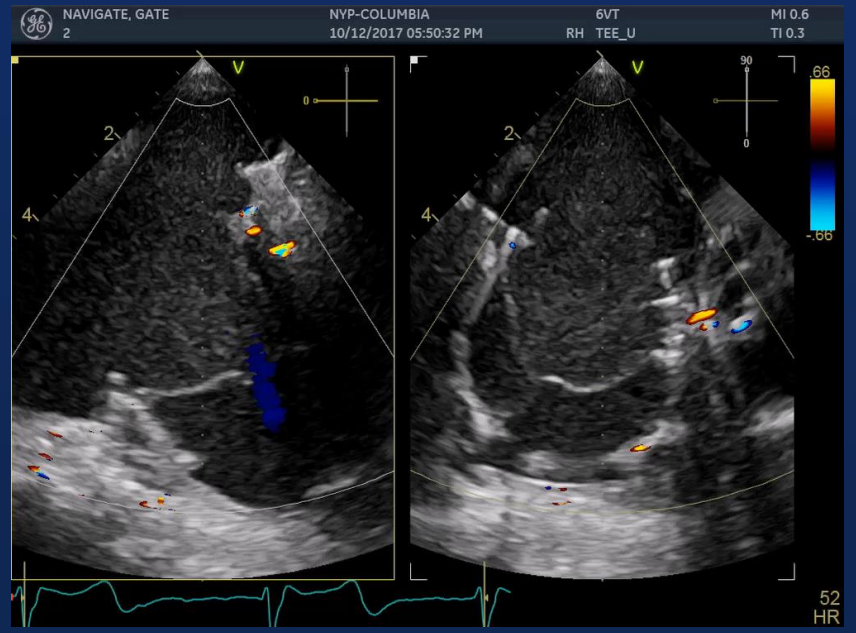




# Final Result

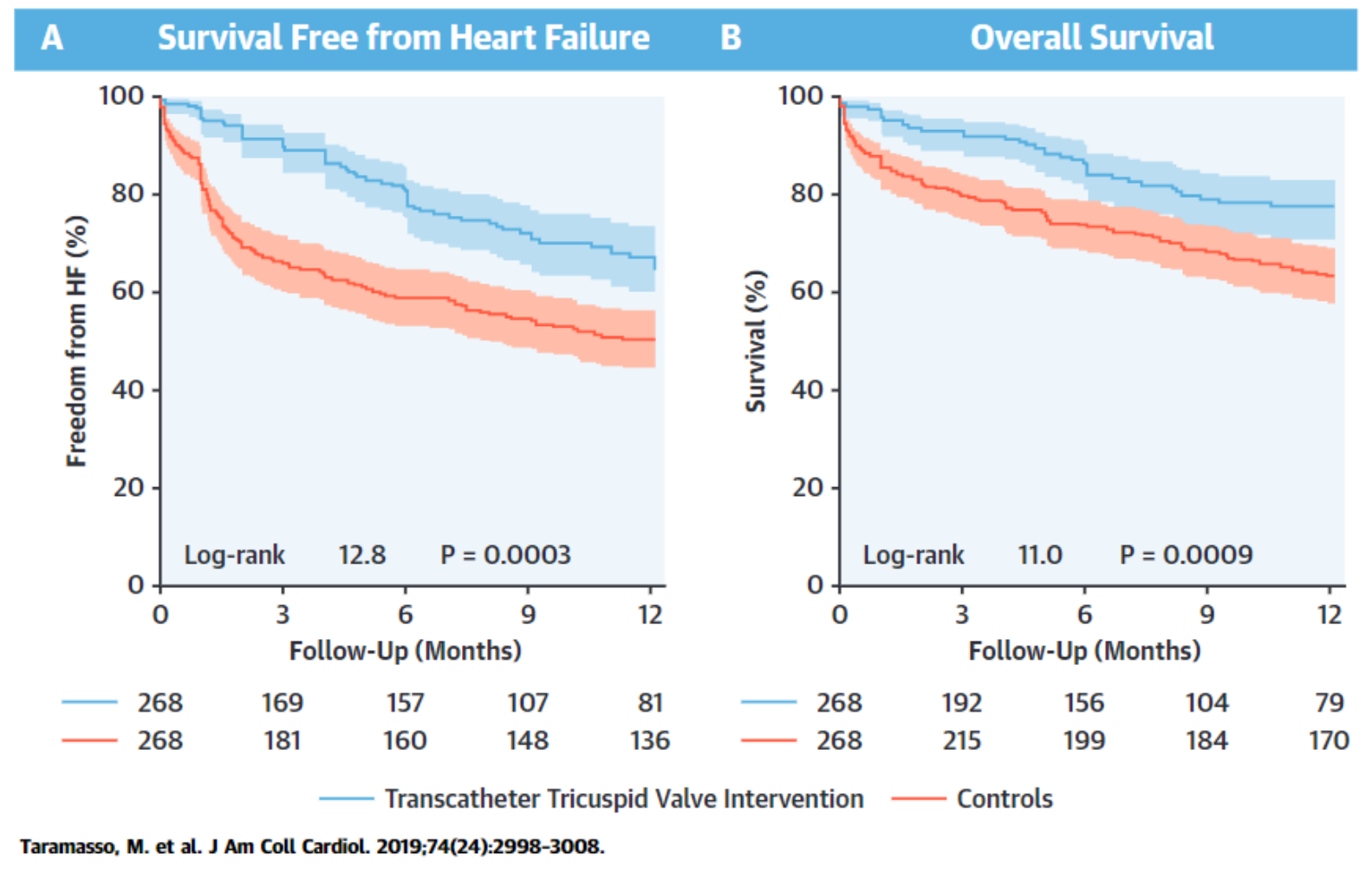





- Trivial central and trivial paravalvular regurgitation
- Peak/mean transtricuspid gradient = 1.5 and 0.3 mmHg

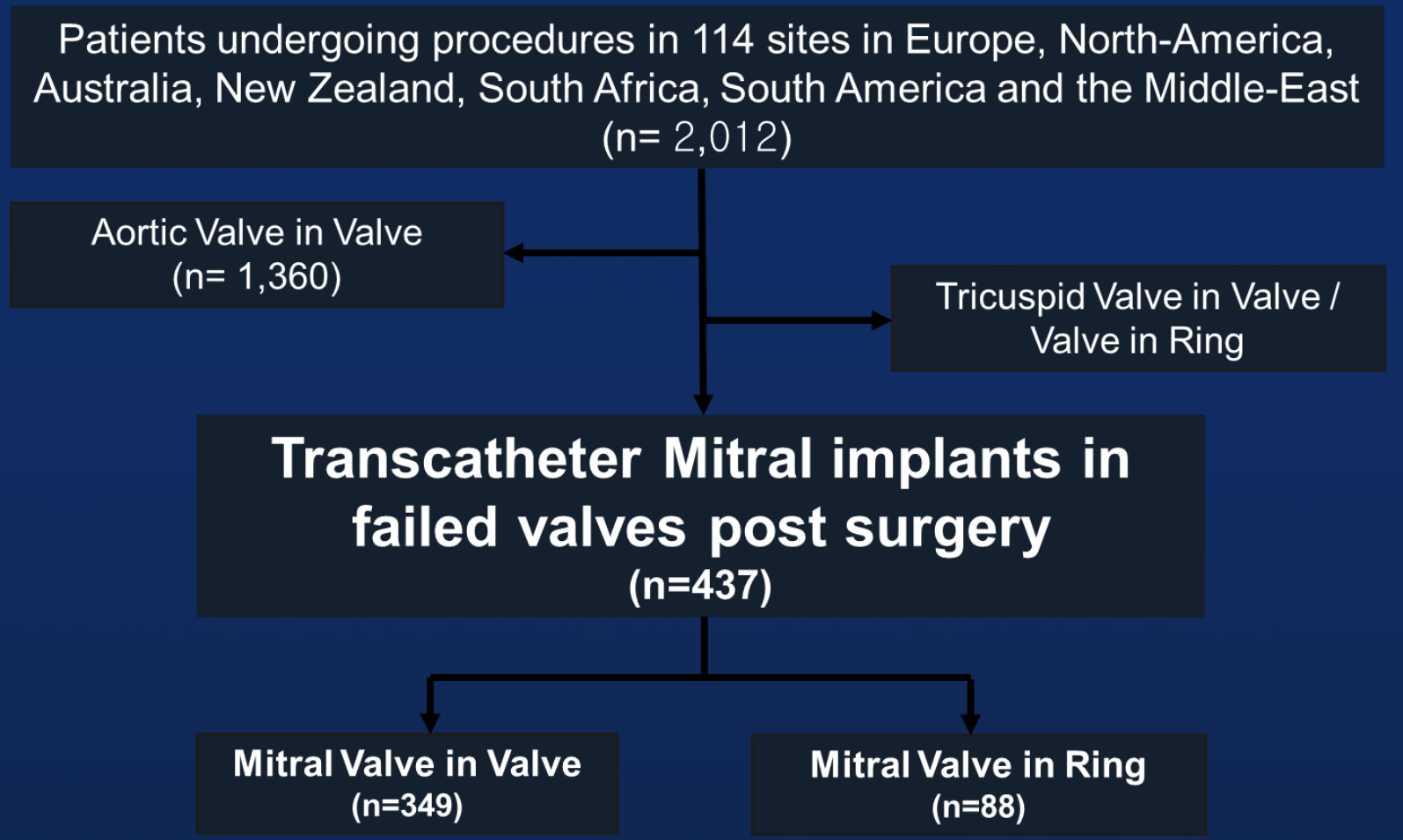
# Outcomes : Transcatheter *vs.* Medical treatment



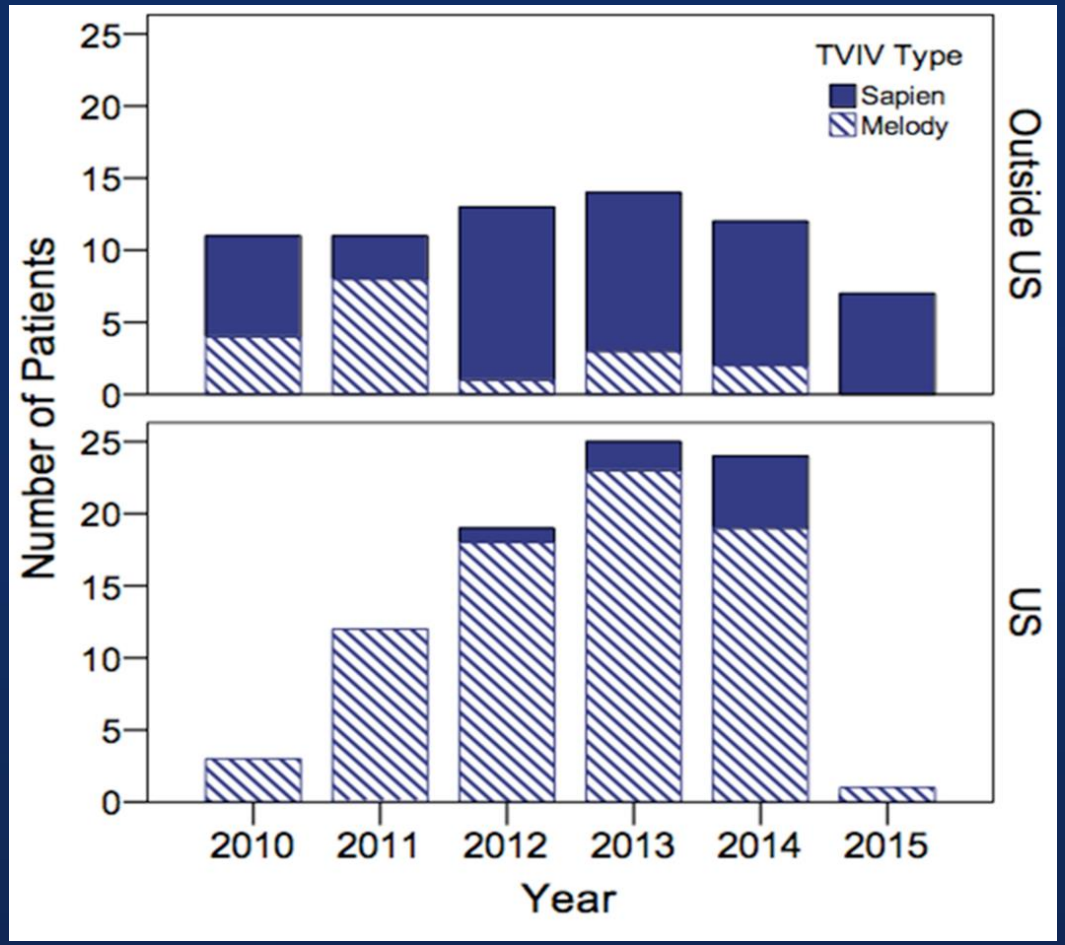

Taramasso, M. et al. J Am Coll Cardiol. 2019;74(24):2998-3008.

# 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.

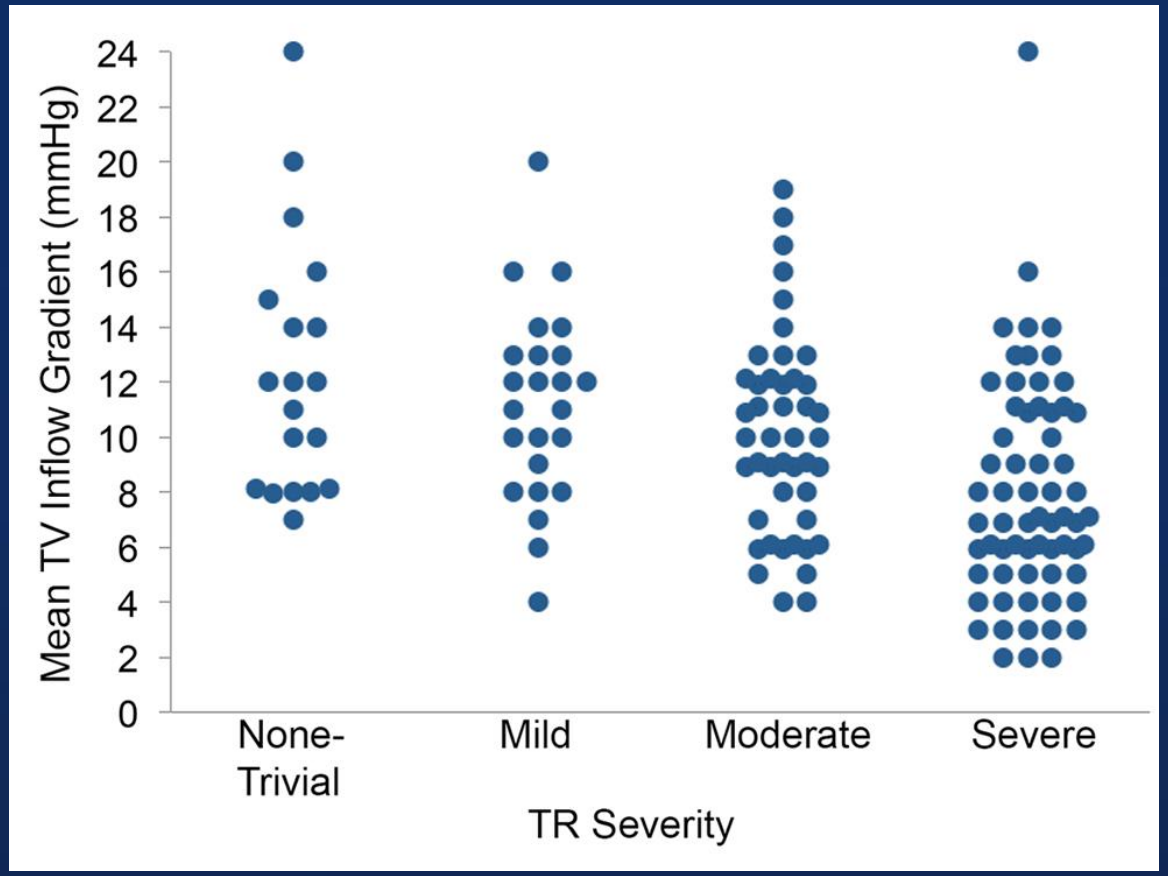
# VIVID Registry –TVIV
## TV function and Prosthesis-Related Data

| 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

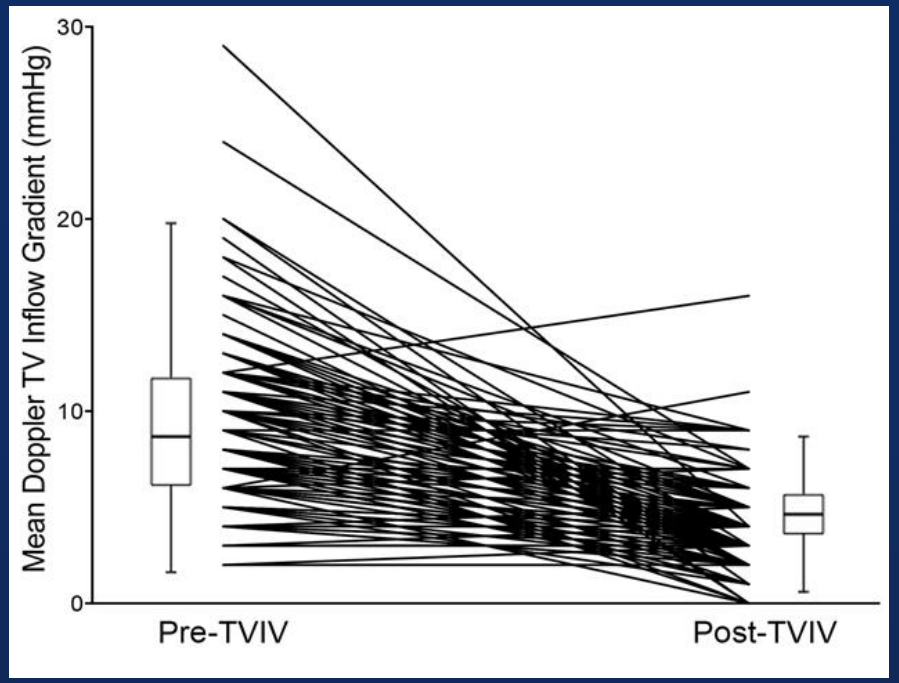


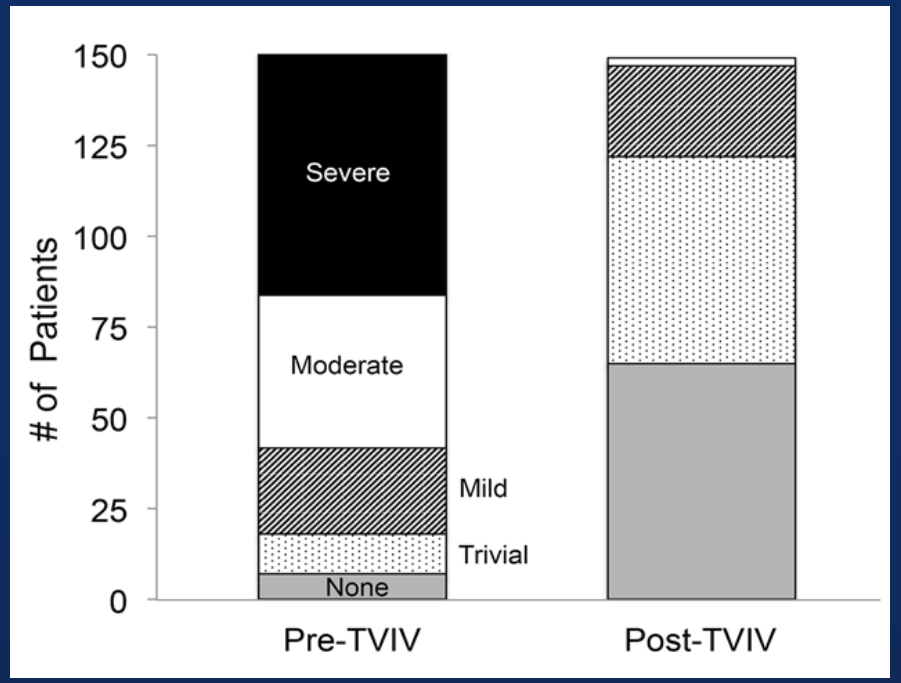

McElhinney D et al. Circulation. 2016;133:1582-1593.

# 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 |

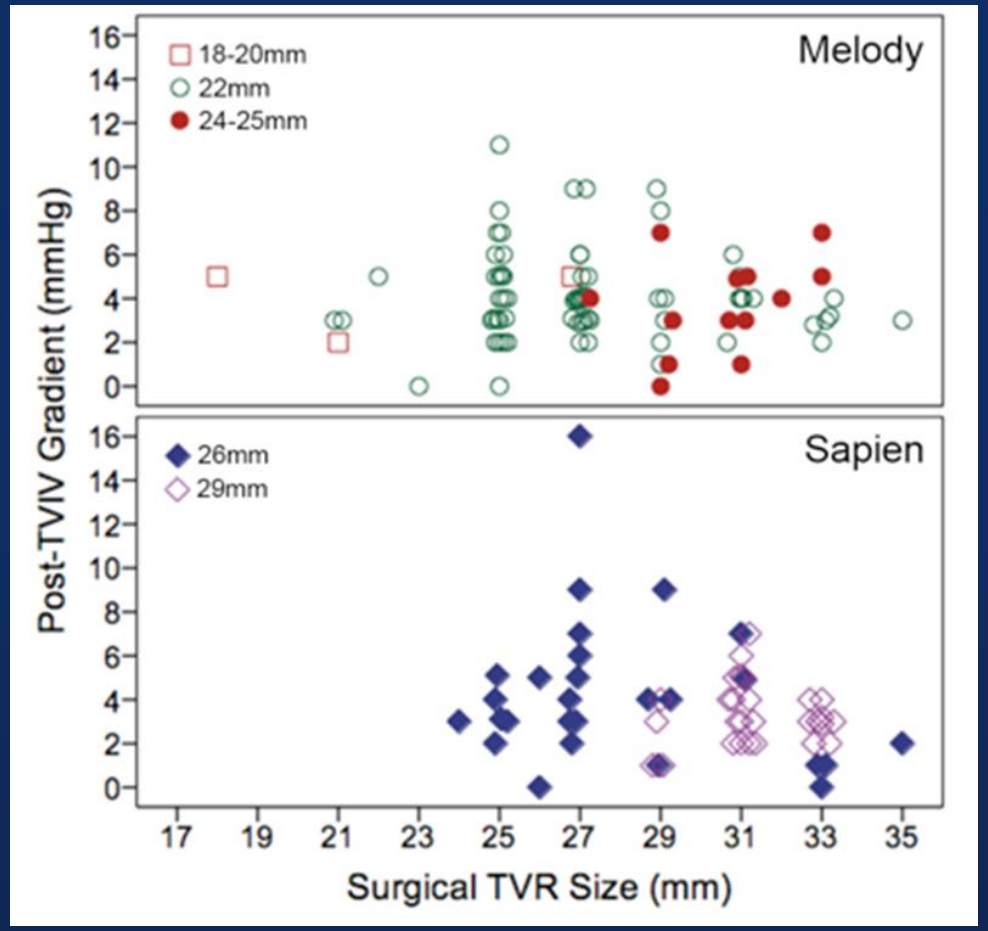
# VIVID Registry –TVIV
## Mean Doppler RA-RV gradient



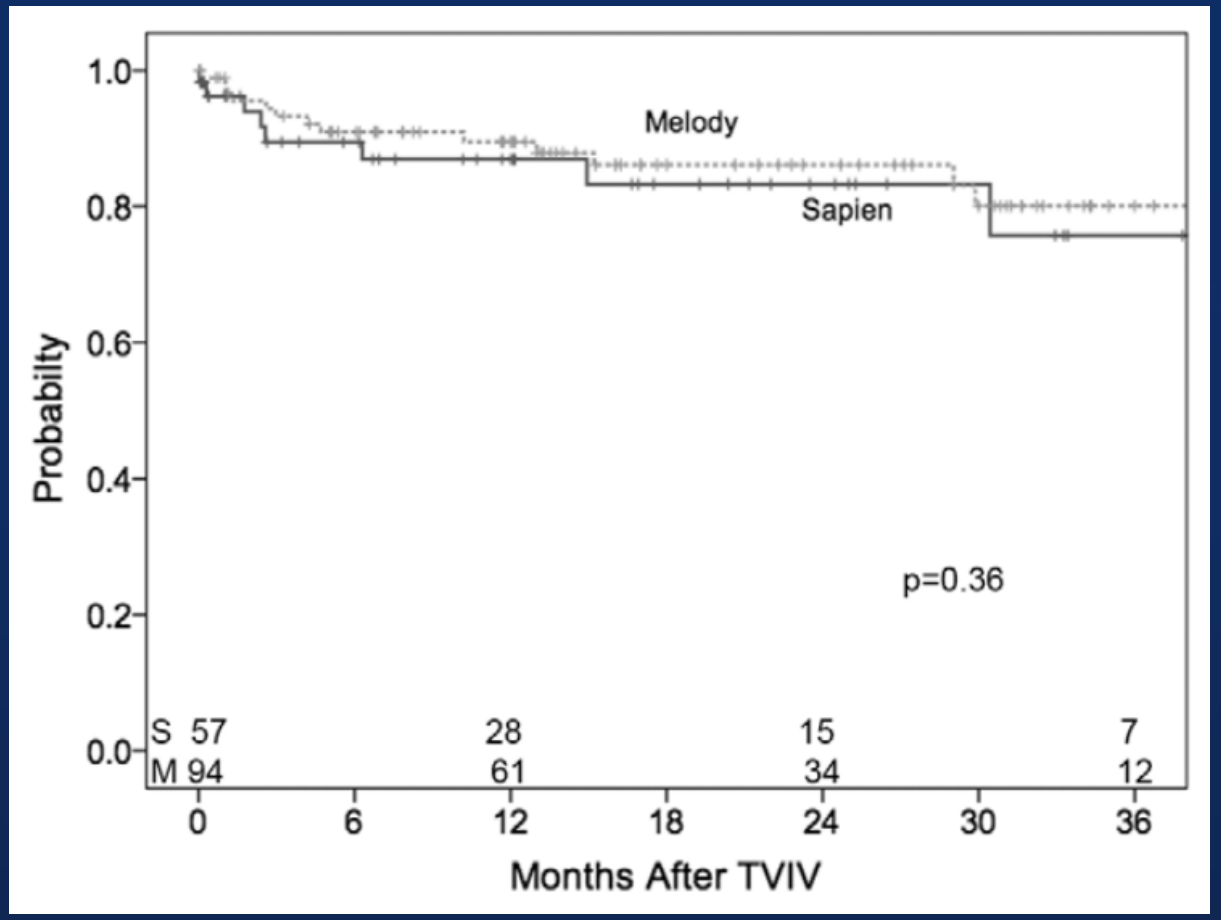

McElhinney D et al. Circulation. 2016;133:1582-1593.

# VIVID Registry –TVIV
## Post-TVIV RA-RV gradient



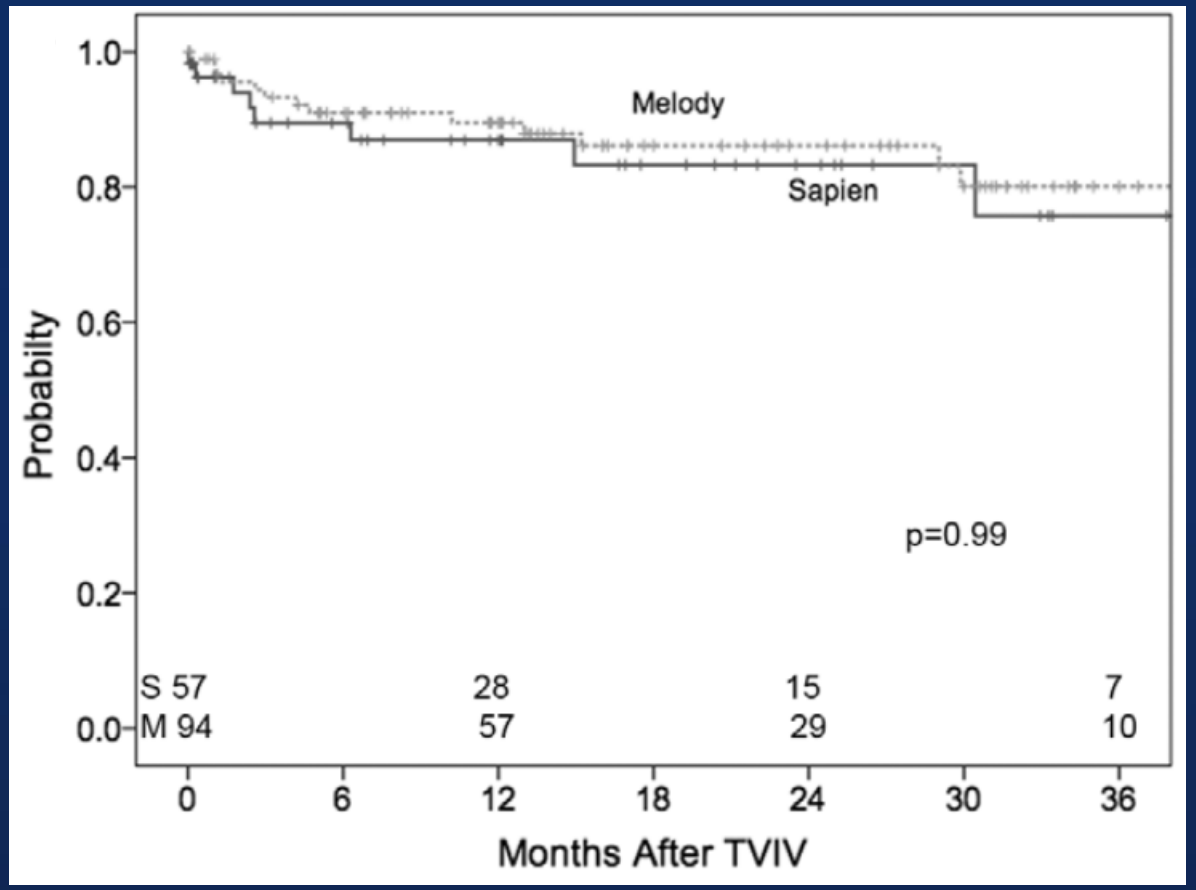

McElhinney D et al. Circulation. 2016;133:1582-1593.

# VIVID Registry –TVIV
## Survival after Tricuspid ViV



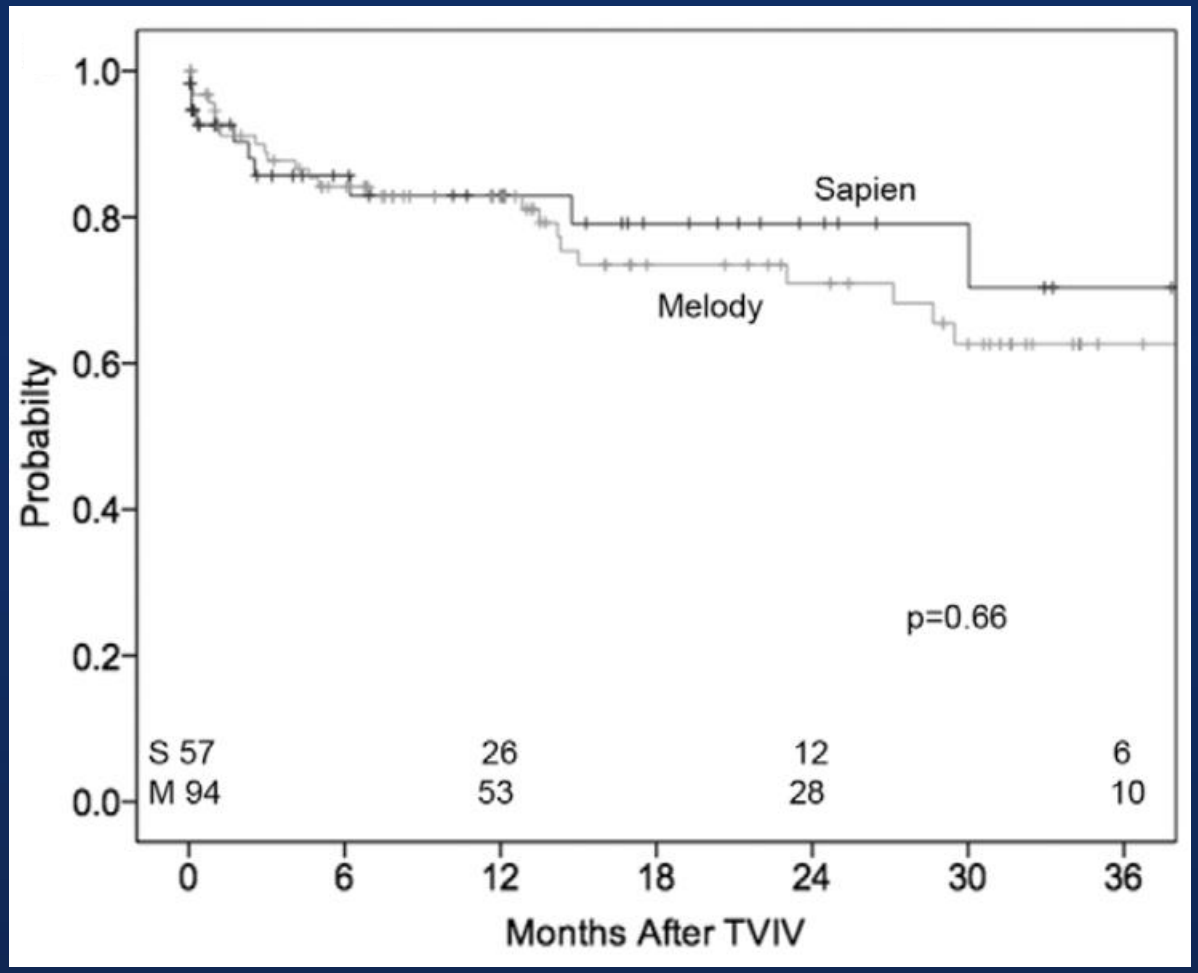

McElhinney D et al. Circulation. 2016;133:1582-1593.

# 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

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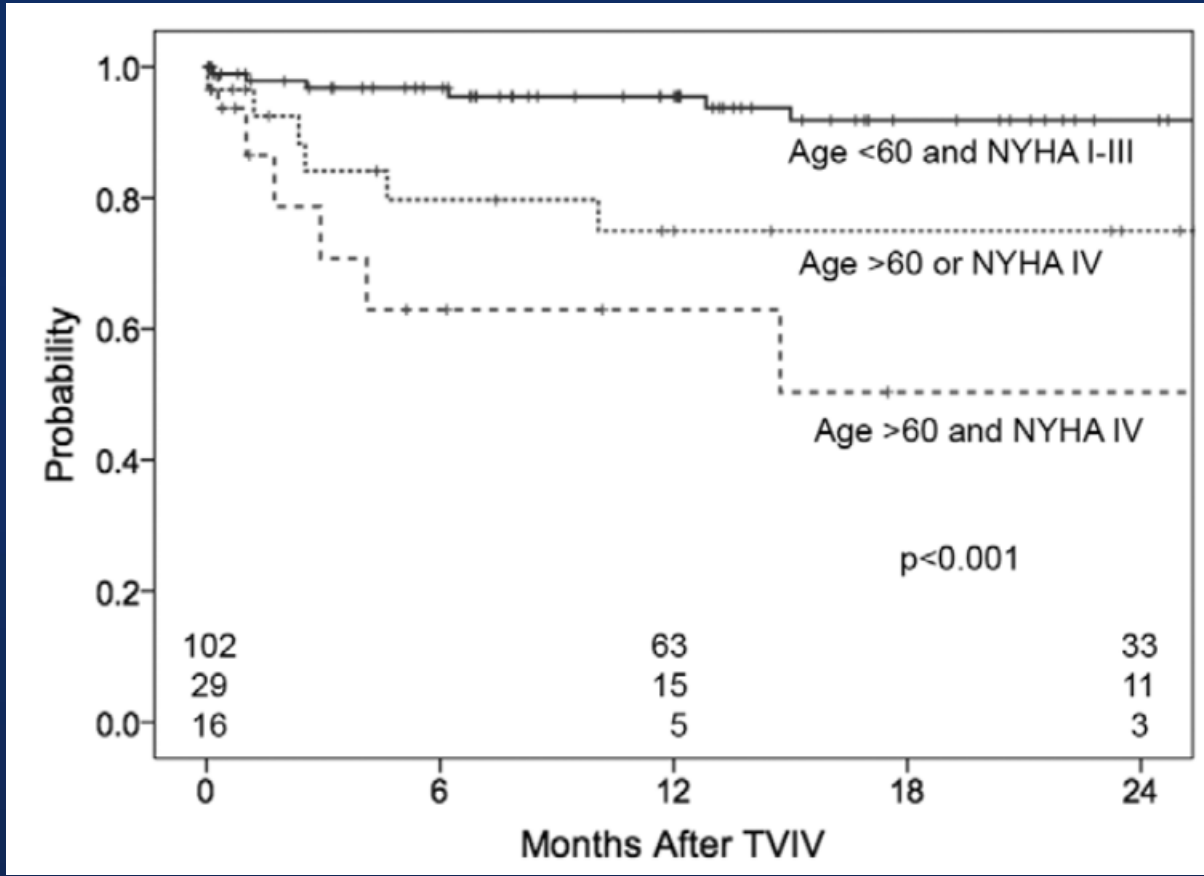
# VIVID Registry –TVIV
## Survival after Tricuspid ViV

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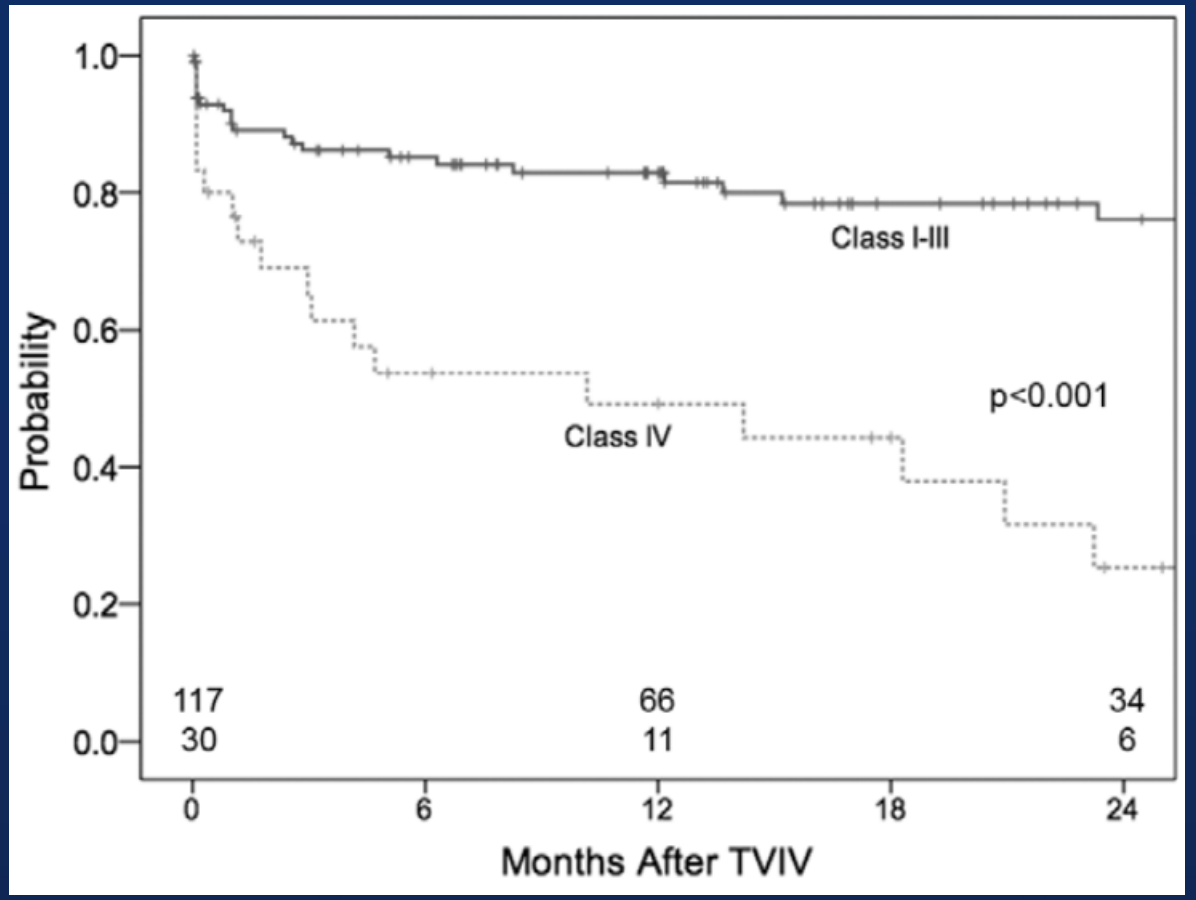



McElhinney D et al. Circulation. 2016;133:1582-1593.

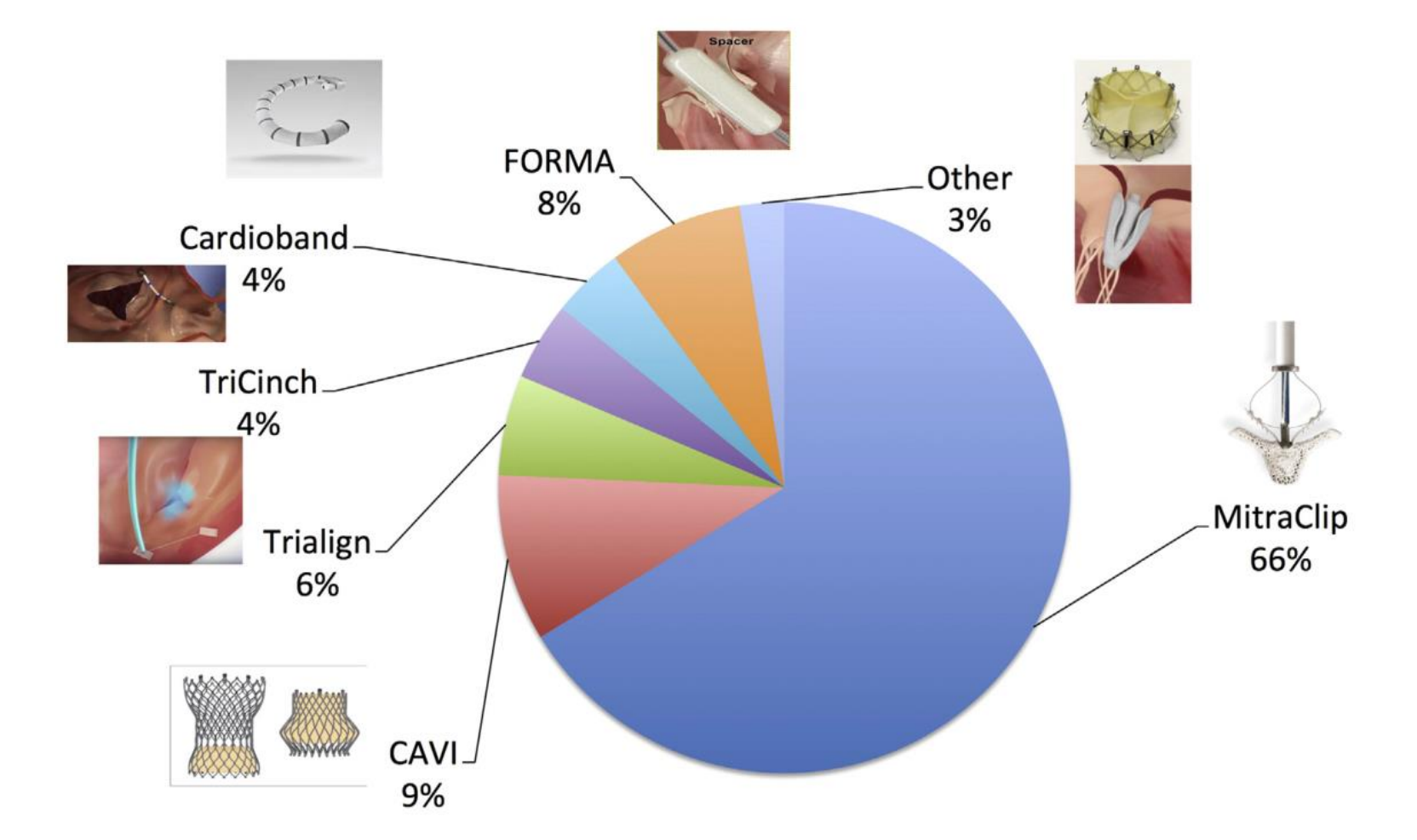
# VIVID Registry –TVIV
## Summary

- 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

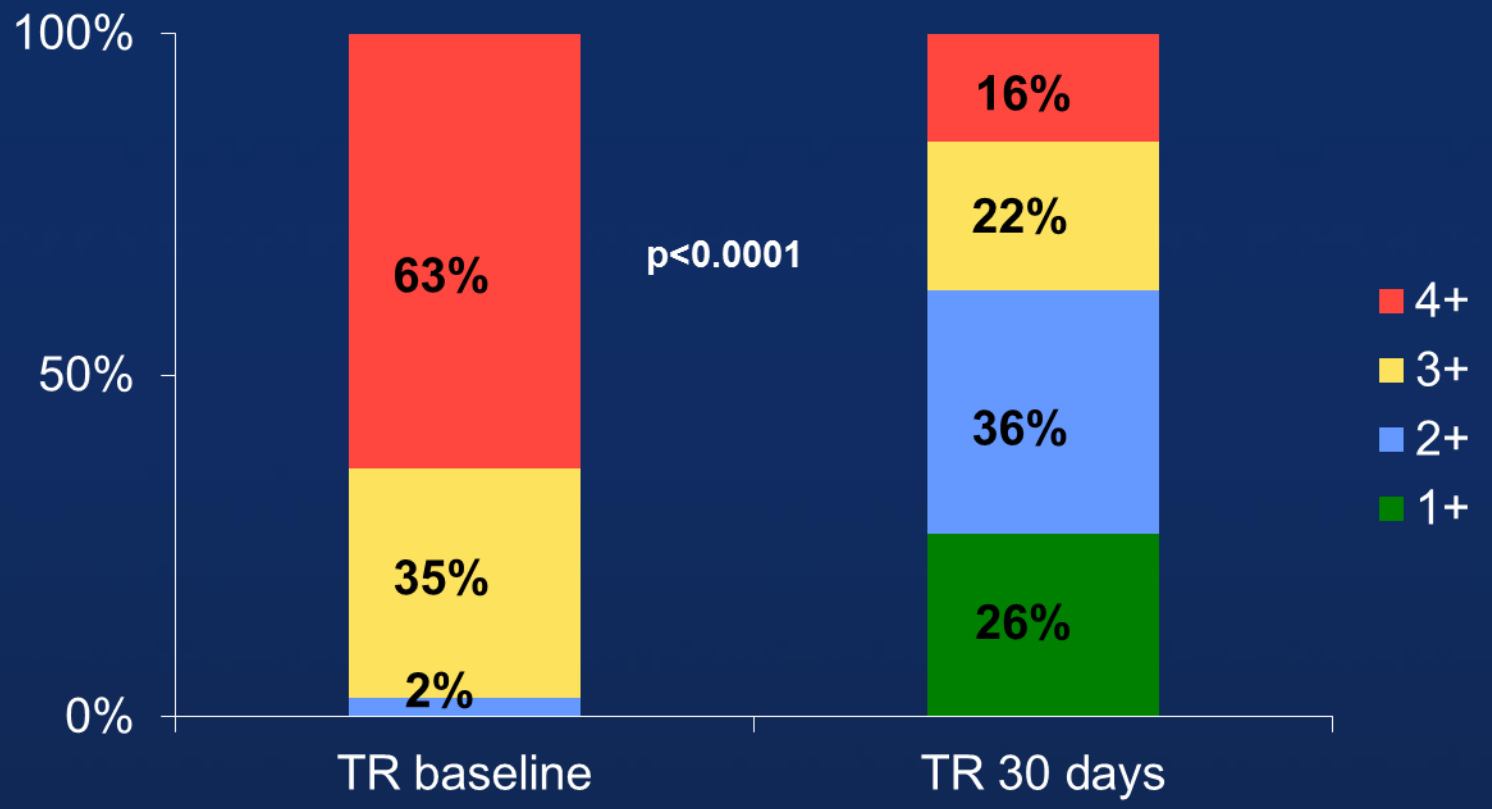
| | N=280 |
|---|---|
| Procedural Success | 204 (72.8) |
| Thirty-day Mortality | 10 (3.6) |
| Major bleeding | 5 (1.7) |
| Stroke | 3 (1.0) |
| Myocardial infarction requiring right coronary artery stenting | 2 (0.7) |
| Conversion to surgery | 4 (1.4) |
| Respiratory failure | 2 (0.7) |
| Device detachment | 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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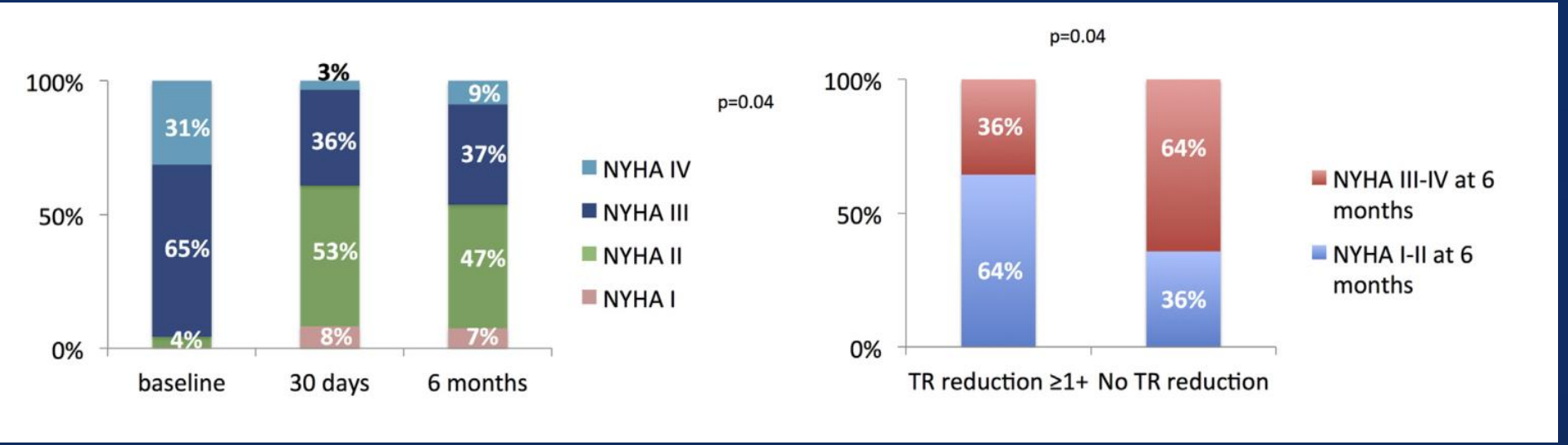
# Transcatheter Therapies for TR
## Changes in Functional Status




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

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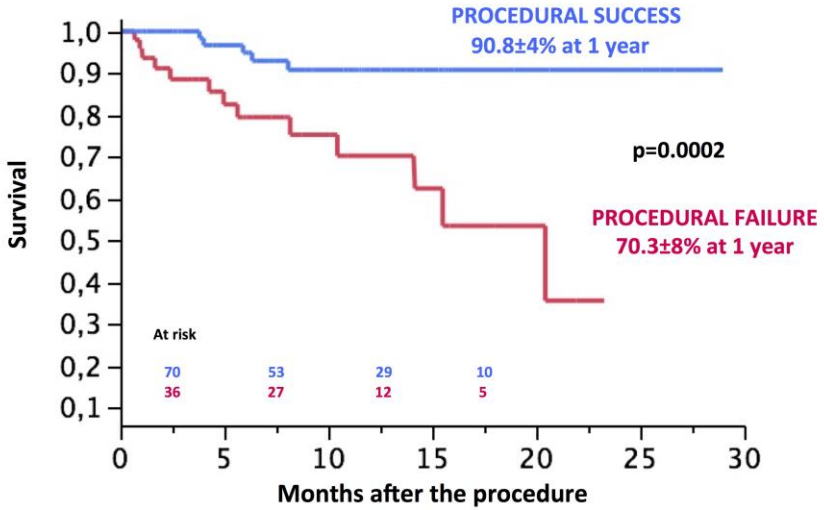
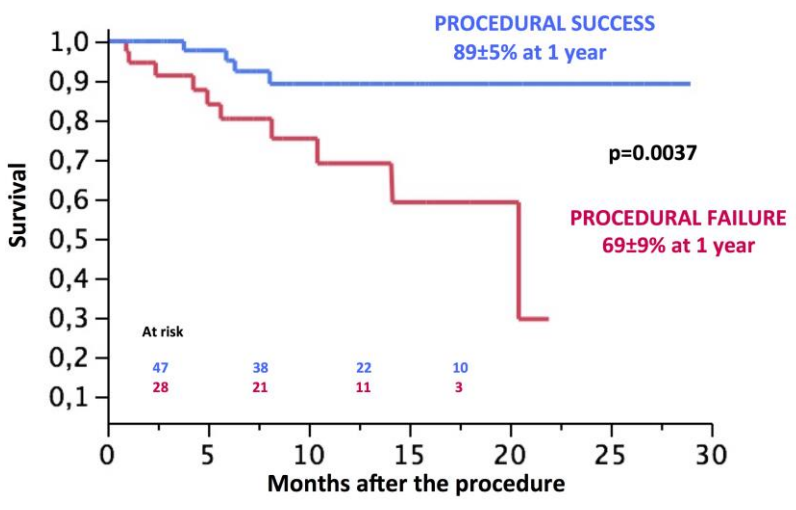
# TriValve Registry
## Follow-up

### 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<br>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<br>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<br>Efficacy: Change of (NYHA) functional class at 6 months |
| Evoque | TRISCEND (NCT04221490) | Early feasibility prospective registry | 200 | Moderate or more | – | Freedom from device or procedure-related adverse events at 30 days |
| | 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<br>- Rate of Major adverse events at 30 days<br>- 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.<br>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<br>Efficacy: technical success and tricuspid regurgitation reduction at 30 days |

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



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