TAVR:
The Year in Review

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TCT-AP 2017– 12 mins

Disclosures

Grant Support/Drugs

- Daiichi-Sankyo
- Astra-Zeneca
- Merck

Grant Support/Devices

- Edwards Lifesciences
- Medtronic
- Biomet
- Abbott Vascular
- Boston Scientific
- CSI

Consulting/Advisory Boards

- Medtronic
- Edwards Lifesciences
- Astra-Zeneca
- Cardinal Health

TAVR Update 2017

- TAVR vs. SAVR in intermediate risk pts
- Stroke prevention
- Valve durability/thrombosis

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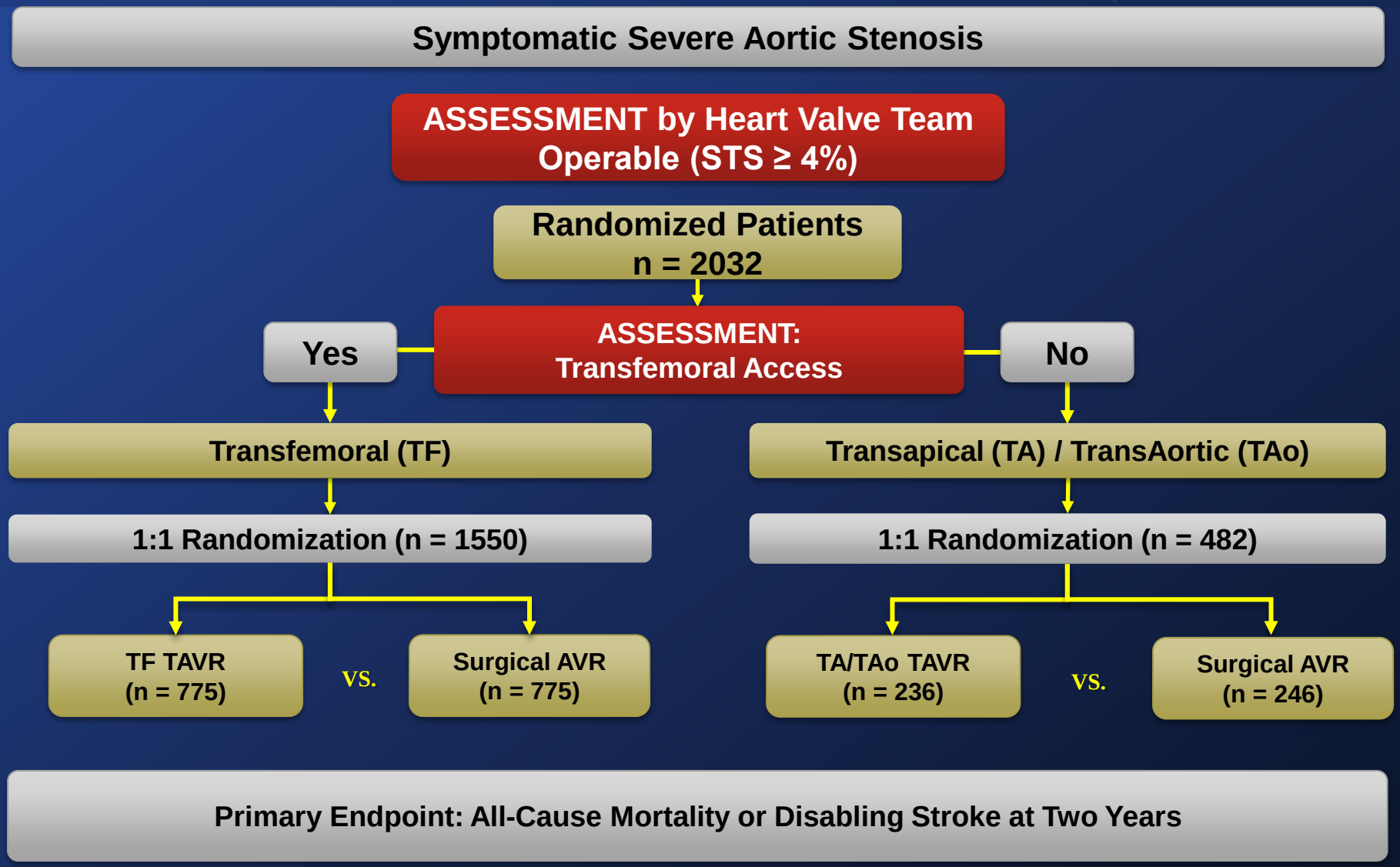
The PARTNER 2A Trial
Study Design

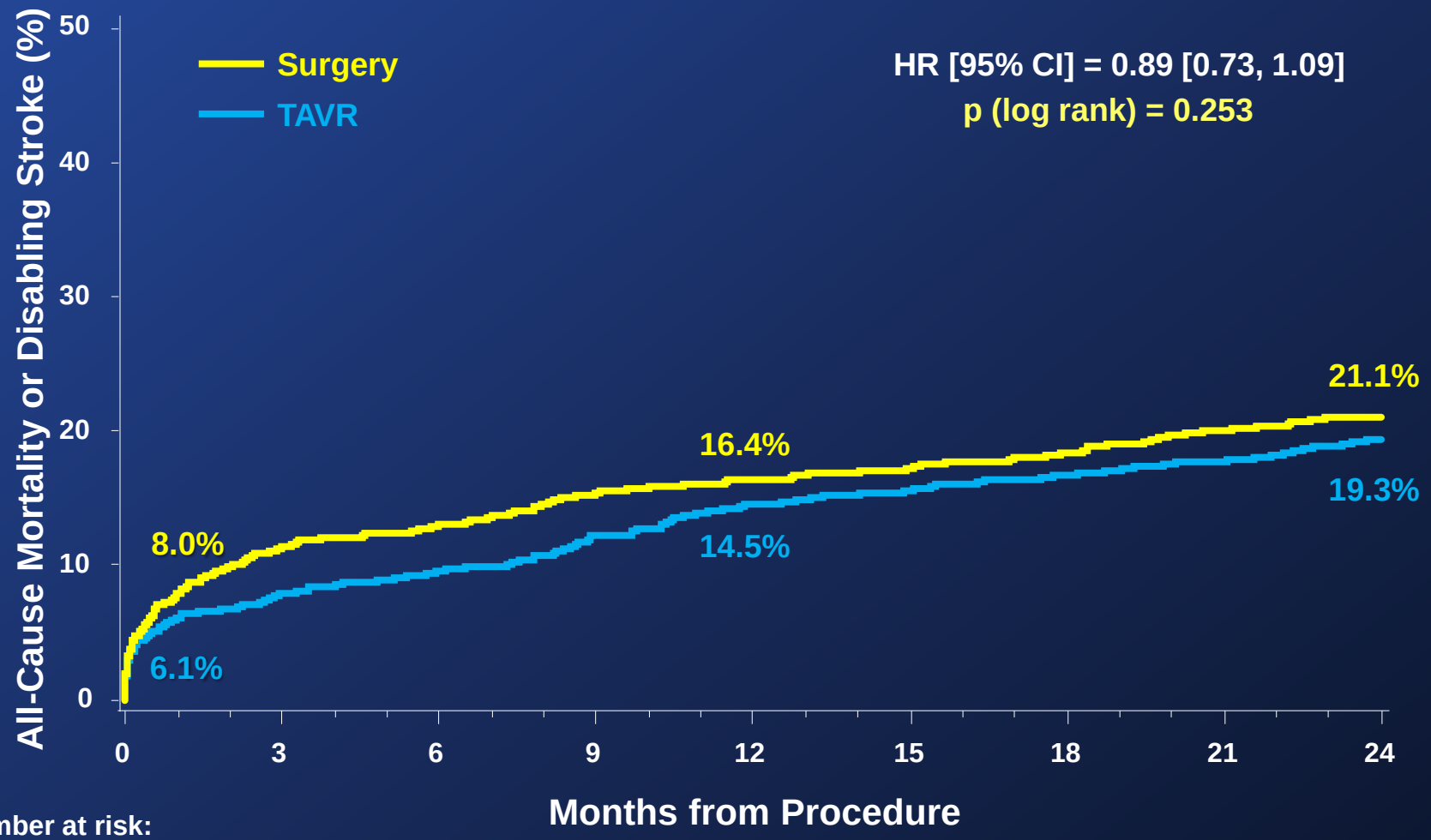


Baseline Patient Characteristics
Demographics and Vascular Disease

THE PARTNER II TRIAL

Characteristic	TAVR (n = 1011)	Surgery (n = 1021)	p-value
Age - yrs	81.5 ± 6.7	81.7 ± 6.7	0.63
Male - %	54.2	54.8	0.79
STS Score - %	5.8 ± 2.1	5.8 ± 1.9	0.29
NYHA Class III or IV - %	77.3	76.1	0.53
CAD - %	69.2	66.5	0.20
Prior CABG - %	23.6	25.6	0.33
Cerebrovascular Disease - %	32.1	31.0	0.60
PVD - %	27.9	32.9	0.02

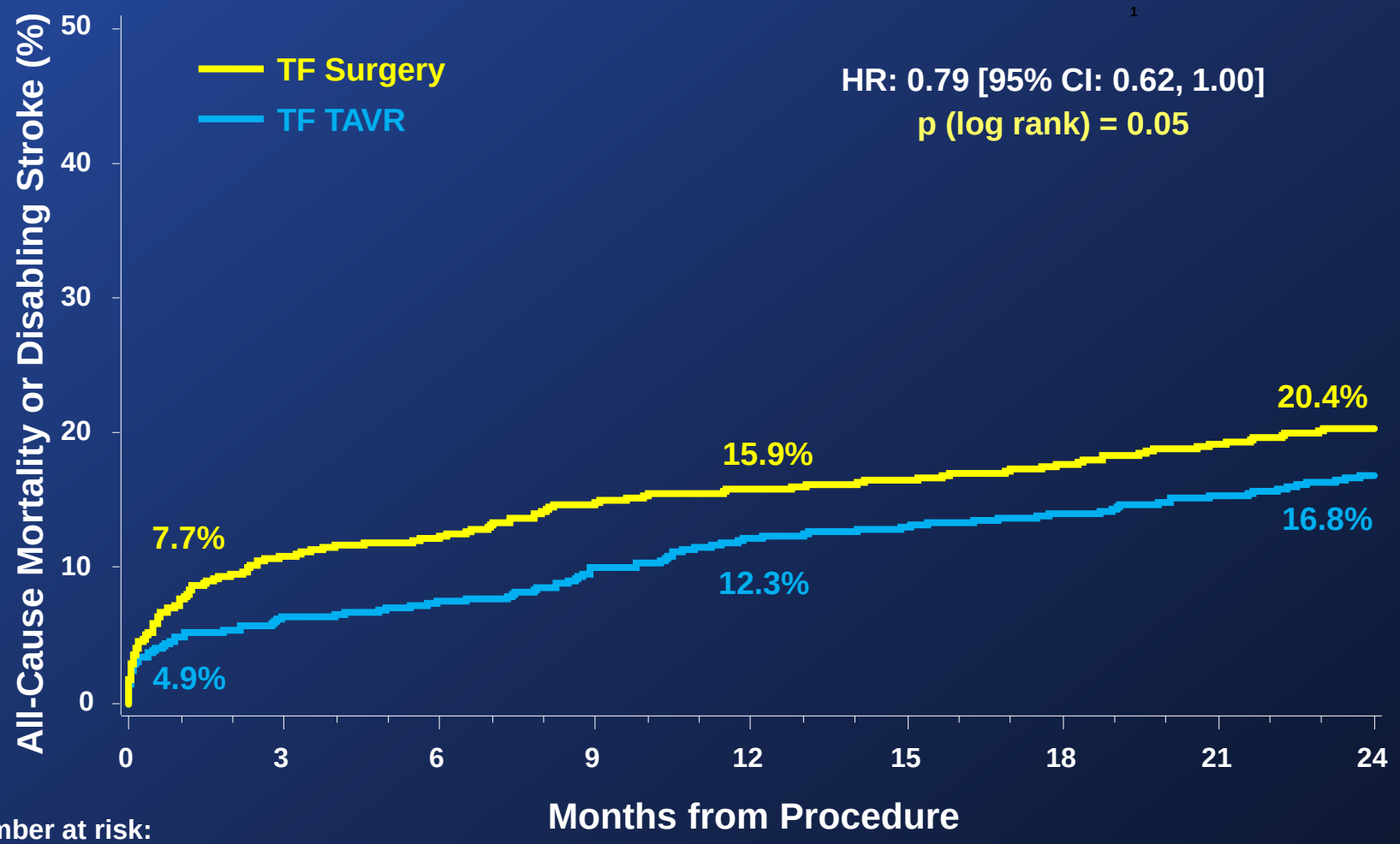
Primary Endpoint (ITT)
All-Cause Mortality or Disabling Stroke



Number at risk:

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

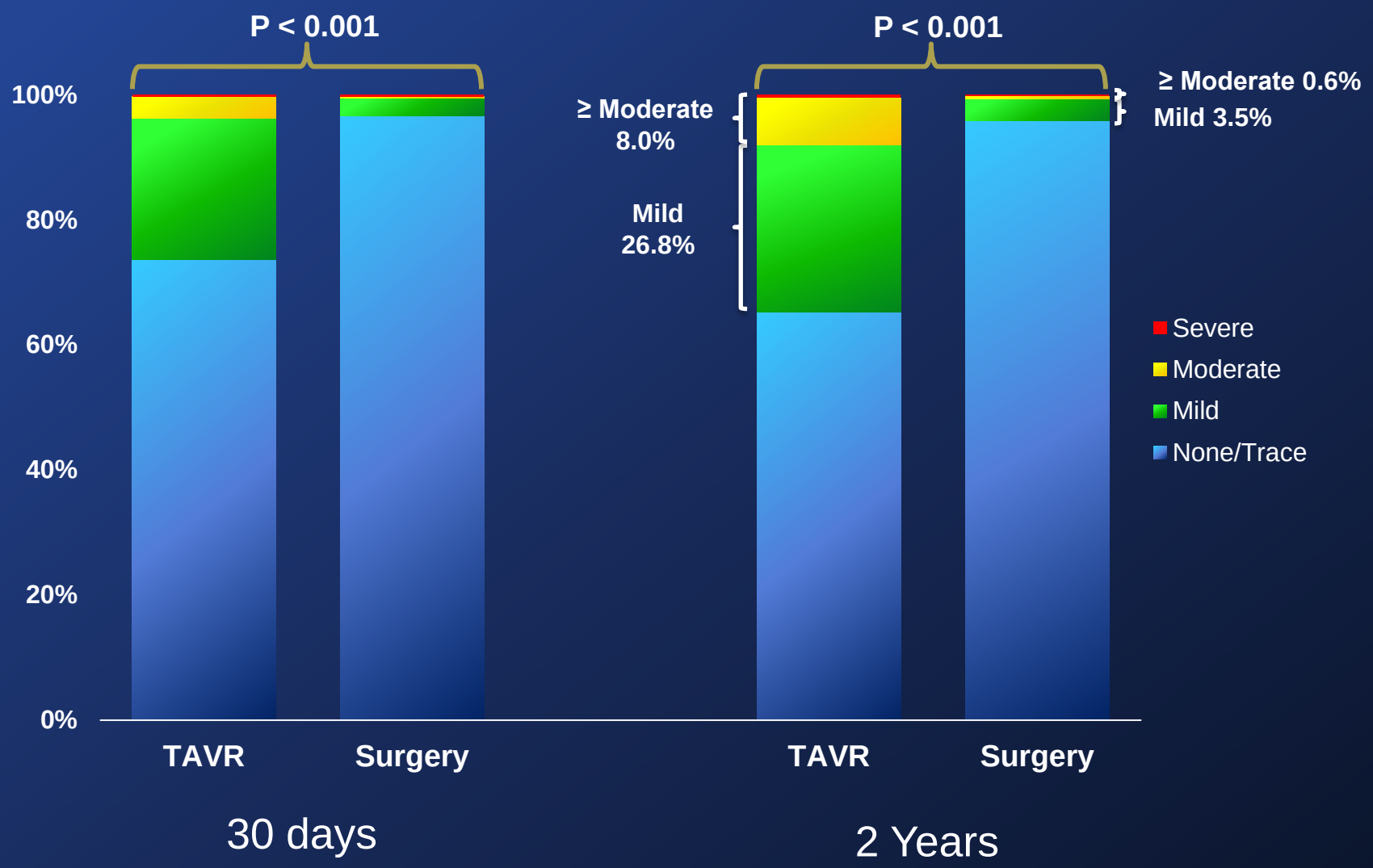
TF Primary Endpoint (ITT)
All-cause Mortality or Disabling Stroke



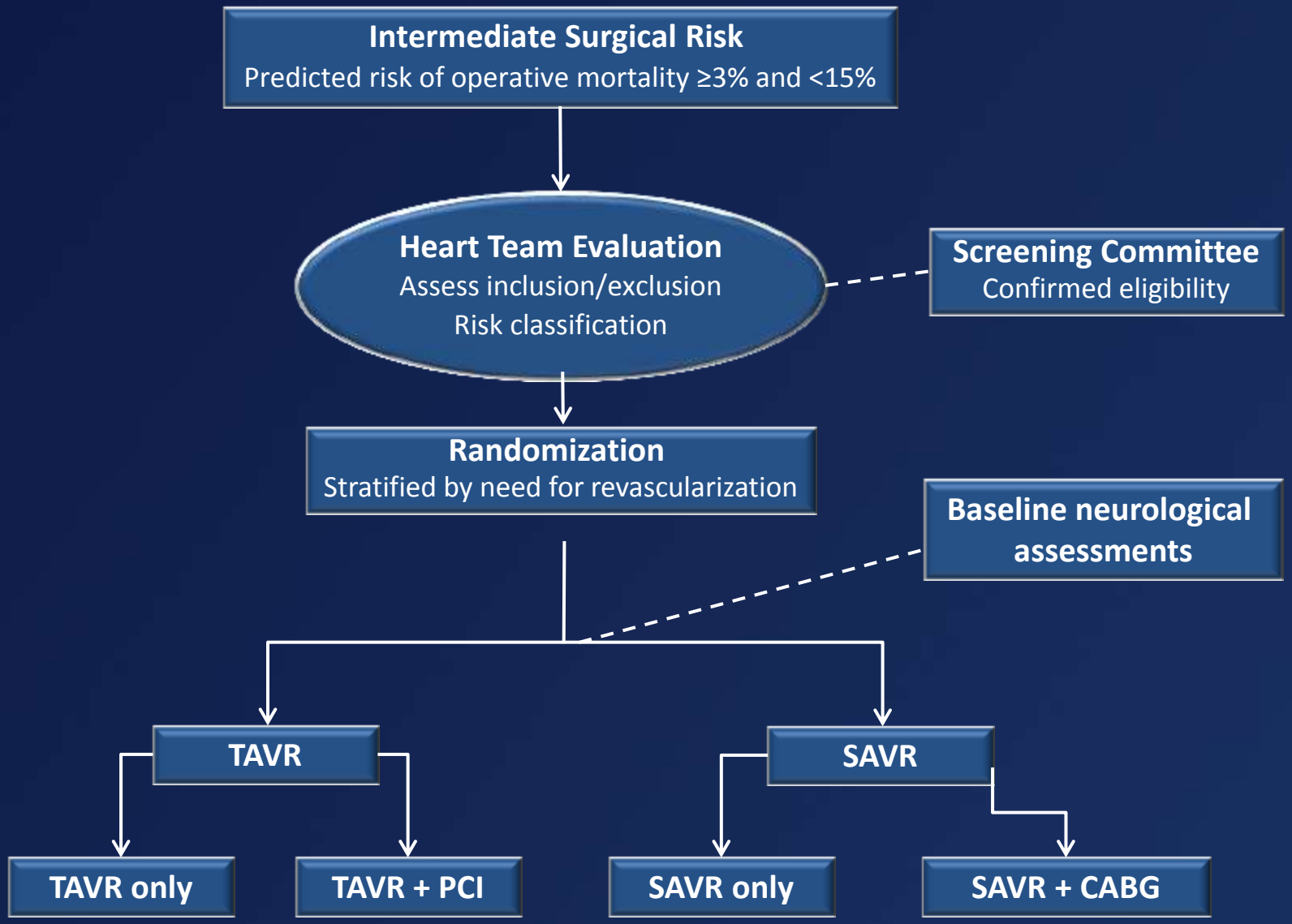
Number at risk:

TF Surgery	775	643	628	604	595	577	569	557	538
TF TAVR	775	718	709	685	663	652	644	634	612

Paravalvular Regurgitation (VI) 3-Class Grading Scheme



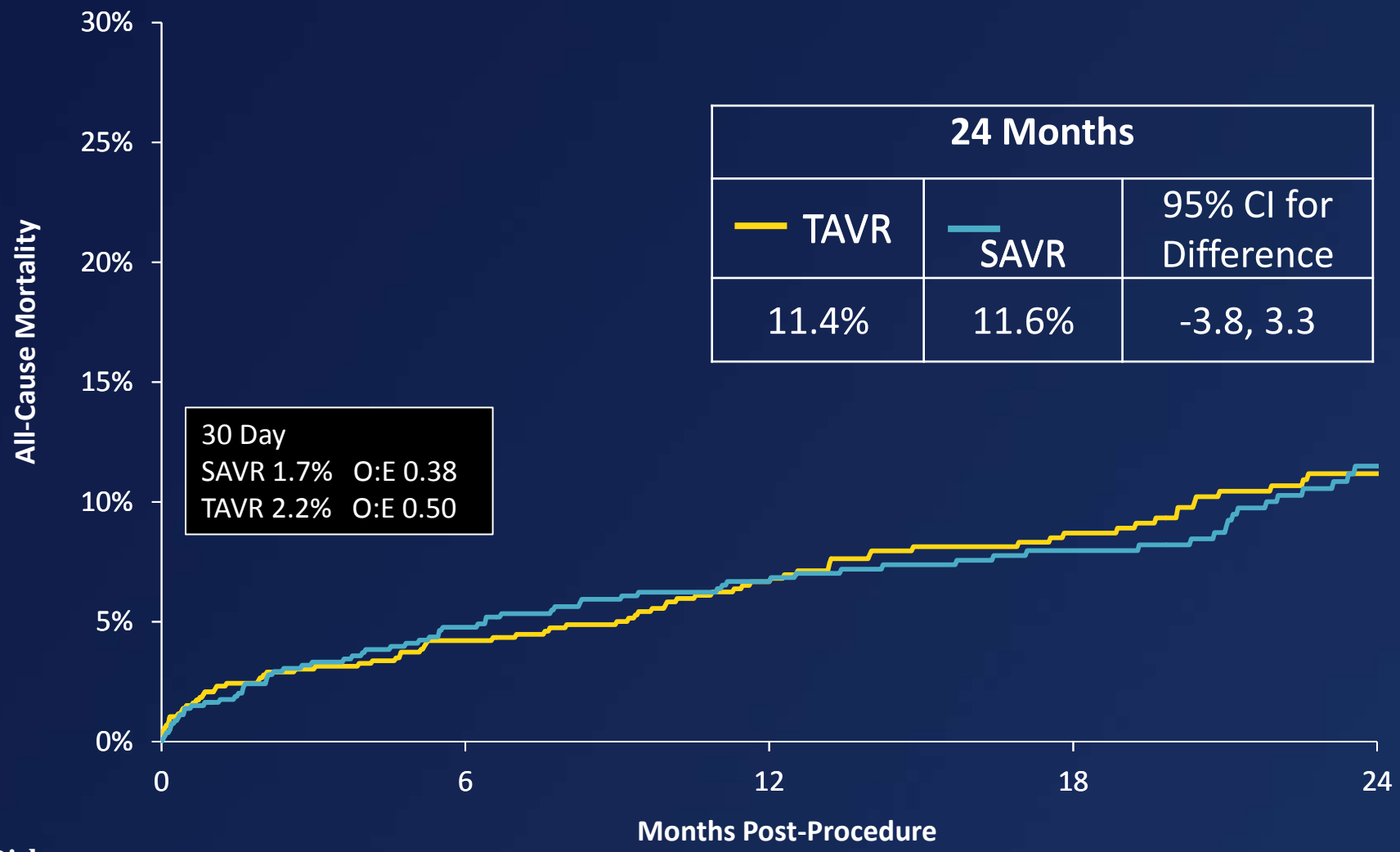
Trial Design



Baseline Characteristics

	TAVR (N=864)	SAVR (N=796)
Age, years	79.9 ± 6.2	79.7 ± 6.1
Male sex	498 (57.6)	438 (55.0)
Body surface area, m^2	1.9 ± 0.2	1.9 ± 0.2
STS PROM, %	4.4 ± 1.5	4.5 ± 1.6
Logistic EuroSCORE, %	11.9 ± 7.6	11.6 ± 8.0
Diabetes mellitus	295 (34.1)	277 (34.8)
Serum creatinine >2 mg/dl	14 (1.6)	17 (2.1)
Prior stroke	57 (6.6)	57 (7.2)
Prior TIA	58 (6.7)	46 (5.8)
Peripheral vascular disease	266 (30.8)	238 (29.9)
Permanent pacemaker	84 (9.7)	72 (9.0)

All-Cause Mortality

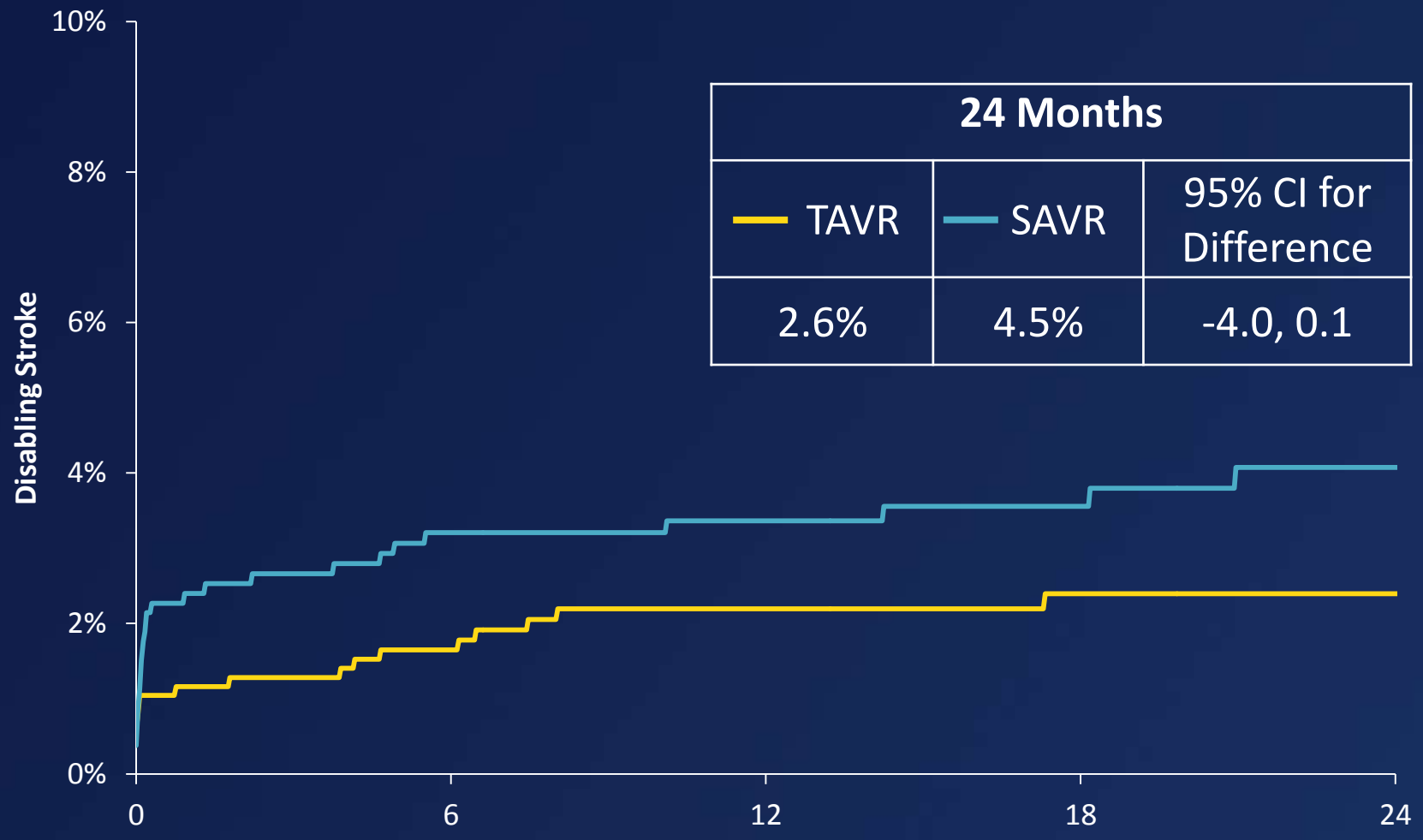


24 Months		
TAVR	SAVR	95% CI for Difference
11.4%	11.6%	-3.8, 3.3

No. at Risk					
SAVR	796	690	569	414	249
TAVR	864	762	621	465	280

Disabling Stroke

CoreValve SURTAVI Trial



24 Months		
TAVR	SAVR	95% CI for Difference
2.6%	4.5%	-4.0, 0.1

No. at Risk					
SAVR	796	674	555	407	241
TAVR	864	755	612	456	272

Summary : TAVR in Intermediate Risk Pts

- Among pts with severe AS and intermediate surgical risk, TAVR results in similar rates of mortality as SAVR– findings that are consistent across both balloon expandable (Sapien-XT) and self-expanding (CoreValve) devices
- Contrary to earlier data, rates of stroke tend to be lower with TAVR than SAVR; these benefits emerge early and are sustained through 2 year f/u
- The main limitation of TAVR vs. SAVR remains PVL, but rates of prognostically important moderate/severe PVL are reasonably low (4-5%)
- More recent device iterations (Sapien-3, EVOLUT-R) appear to lead to even better outcomes– possibly through further reductions in PVL

TAVR Update 2017

- TAVR vs. SAVR in intermediate risk pts
- Stroke prevention
- Valve durability/thrombosis

Claret Medical® Sentinel® Cerebral Protection System

- Dual independent filters for embolic debris capture and removal
- Right transradial 6F sheath access
- Deflectable sheath facilitates cannulation of LCC
- Low profile in aortic arch to minimize interaction with TAVR delivery catheter

The SENTINEL Trial

Patients with Severe Symptomatic Aortic Stenosis Undergoing TAVR

Patients Randomized (1:1:1)
n=363

Safety Cohort

Imaging Cohort

SAFETY ARM
TAVR with Sentinel
(n=123)

TEST ARM
TAVR with Sentinel
(n=121)

CONTROL ARM
TAVR Only
(n=119)

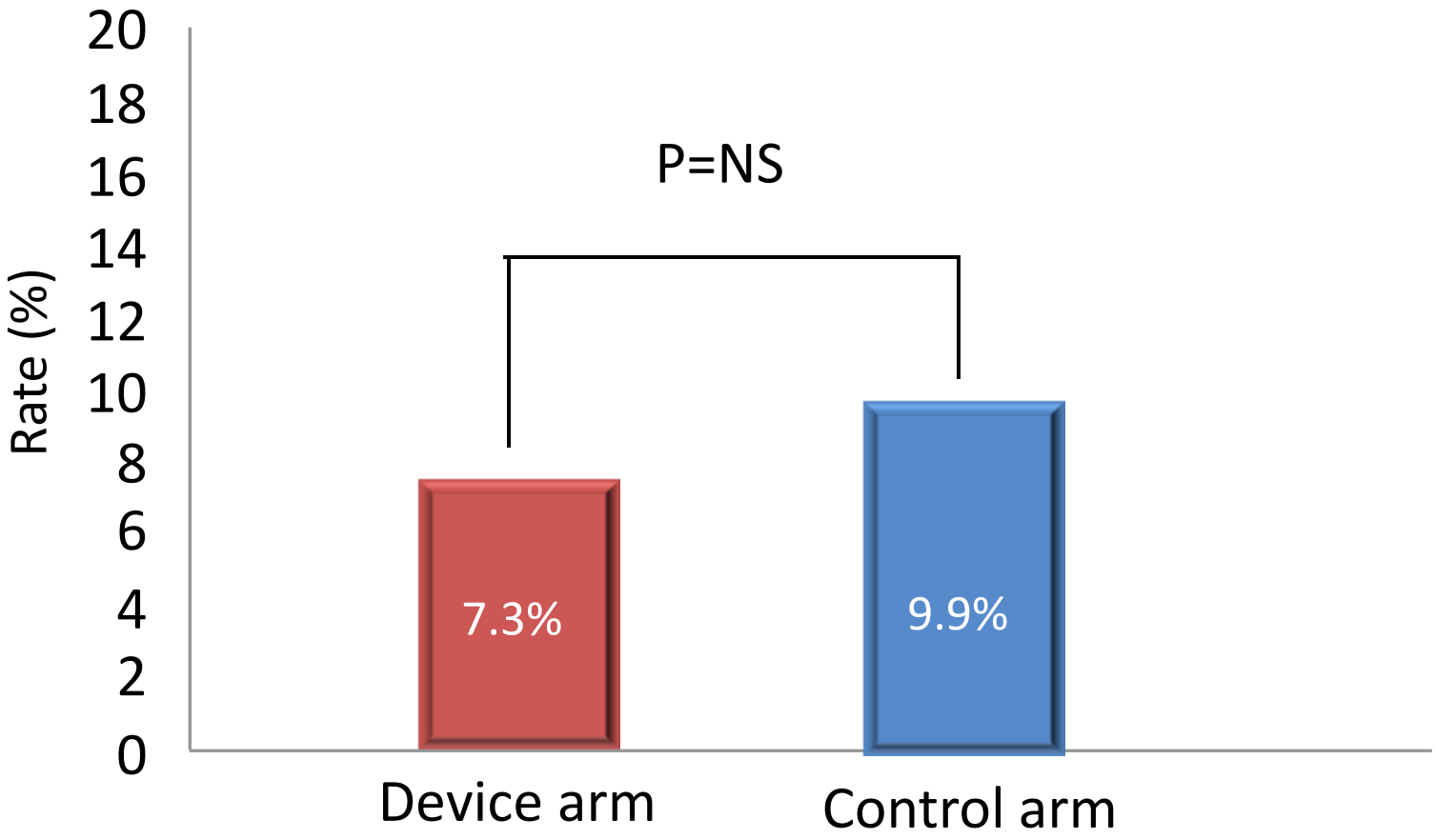
Clinical Follow-Up (Neurologic oversight in all patients)

Serial MRIs (Baseline, Day 2-7 & Day 30)

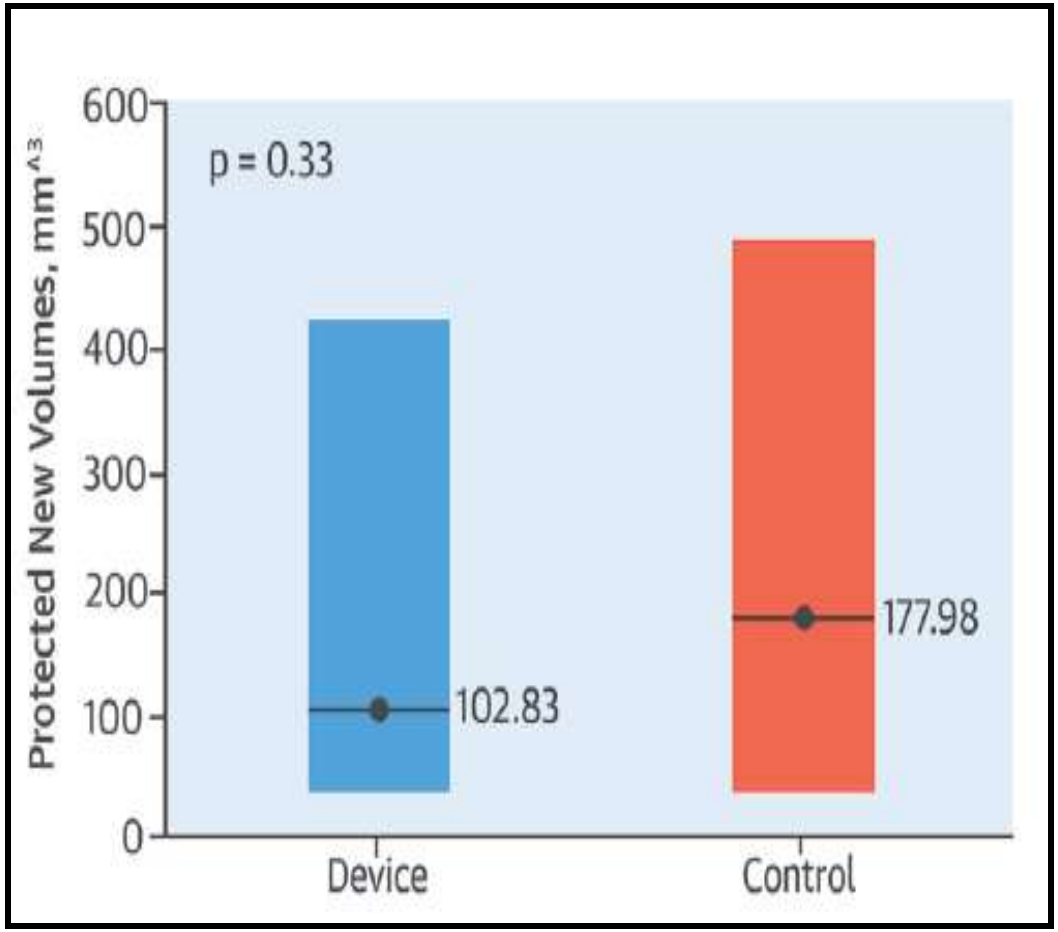
Serial Neurocognitive Assessment (Baseline, Day 30 & Day 90)

Primary Safety Endpoint

30-Day MACCE (Death, Stroke, AKI

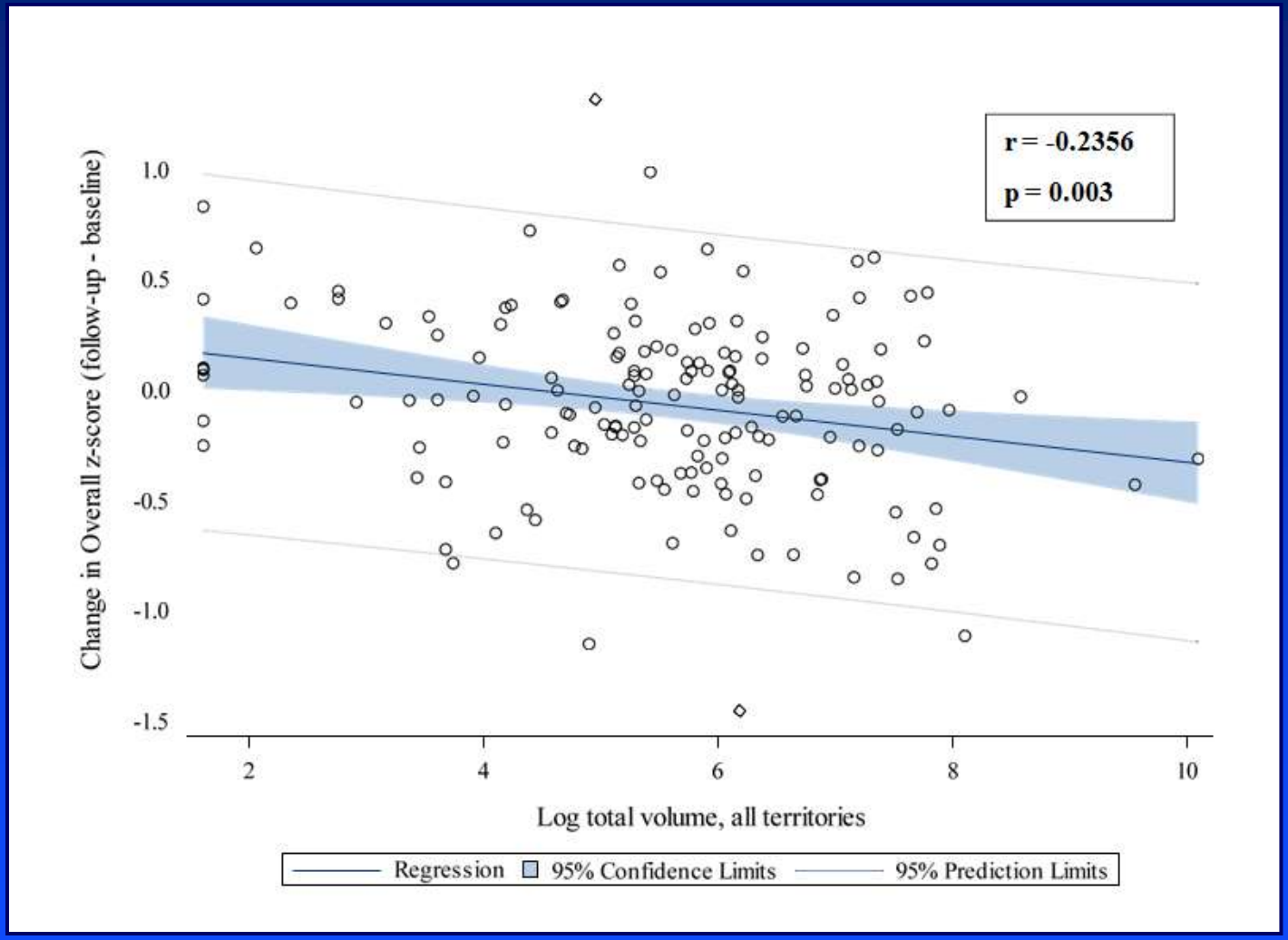


Primary Efficacy Endpoint



- Trend toward benefit, but no overall reduction in new lesion volume in protected territories
- After adjustment for valve type, baseline lesion volume, and valve*treatment interaction, there was a significant benefit of embolic protection– both in protected territories (p=0.025) and overall (p=0.05)

Correlation between New Lesion Volume and Neurocognitive Decline



Kapadia SR, et al. JACC 2017;69:367-77

Embolic Protection in TAVR

- Embolic protection for TAVR remains an attractive concept, given its ability to safely capture embolic debris at the time of TAVR
- Not clear whether stroke reduction is a legitimate goal for these devices, but data on the relationship between CNS lesion volume and neurocognitive decline suggests that lesion volume may be a reasonable surrogate
- Given declining stroke rates with TAVR (and the fact that rates are already lower than with SAVR), it will be interesting to watch whether embolic protection becomes “standard of care” with TAVR or is reserved mainly for high risk patients

TAVR Update 2017

- TAVR vs. SAVR in intermediate risk pts
- Stroke prevention
- Valve durability/thrombosis

Centre for
Heart Valve Innovation
St. Paul's Hospital, Vancouver

2016 euro PCR

First look at long-term durability of transcatheter heart valves:

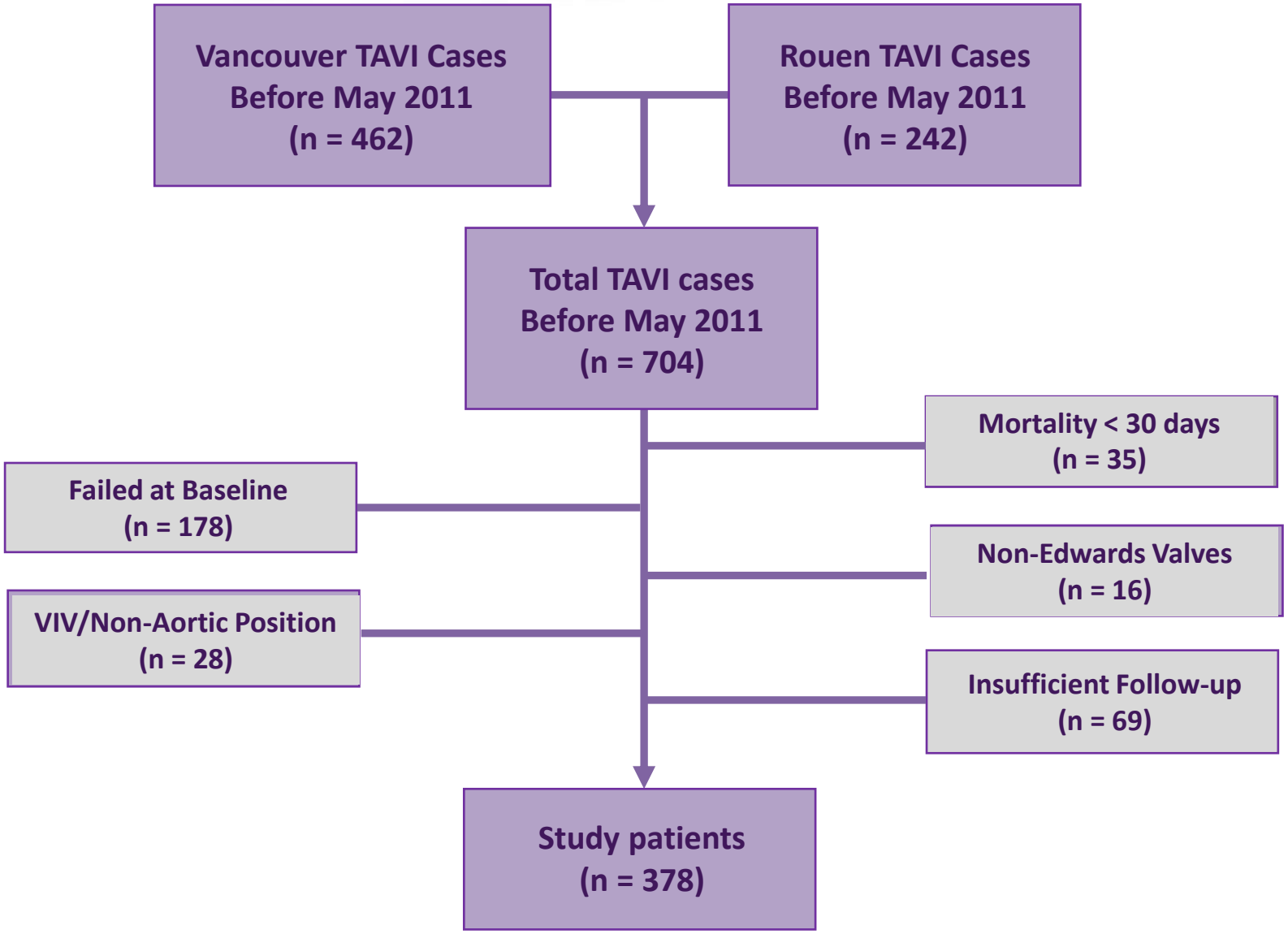
Assessment of valve function up to 10-years after implantation

Danny Dvir, St. Paul's Hospital, Vancouver, Canada.

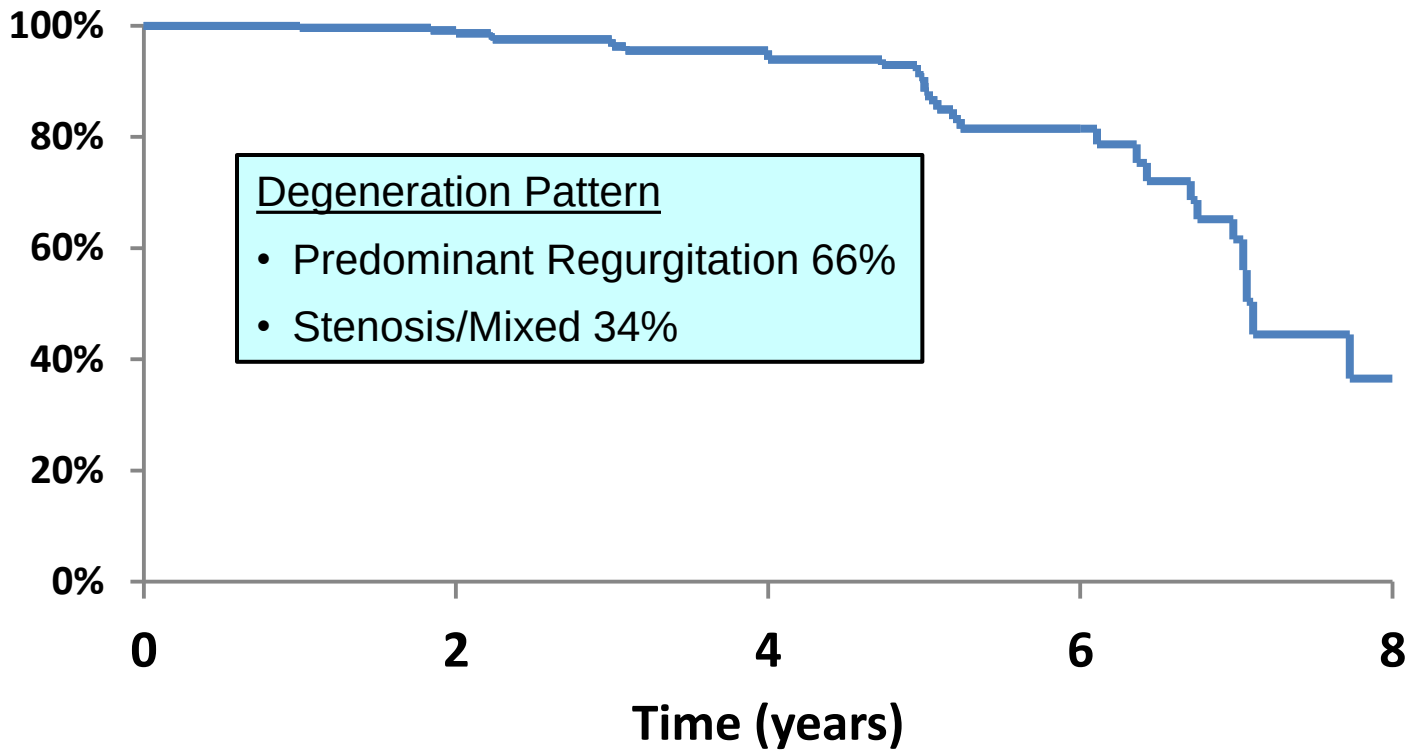
On behalf of coauthors: Helene Eltchaninoff, Jian Ye, Arohumam Kan, Eric Durand, Anna Bizios, Anson Cheung, Mina Aziz, Matheus Simonato, Christophe Tron, Yaron Arbel, Robert Moss, Jonathon Leipsic, Hadas Ofek, Gidon Perlman, Marco Barbanti, Michael A. Seidman, Philippe Blanke, Robert Yao, Robert Boone, Sandra Lauck, Sam Lichtenstein, David Wood, Alain Cribier, John Webb

EAPCI EUROPEAN SOCIETY OF CARDIOLOGY EACTS

Methods


Vancouver TAVI Cases
Before May 2011
(n = 462)
Rouen TAVI Cases
Before May 2011
(n = 242)
Total TAVI cases
Before May 2011
(n = 704)
Mortality < 30 days
(n = 35)
Failed at Baseline
(n = 178)
Non-Edwards Valves
(n = 16)
VIV/Non-Aortic Position
(n = 28)
Insufficient Follow-up
(n = 69)
Study patients
(n = 378)

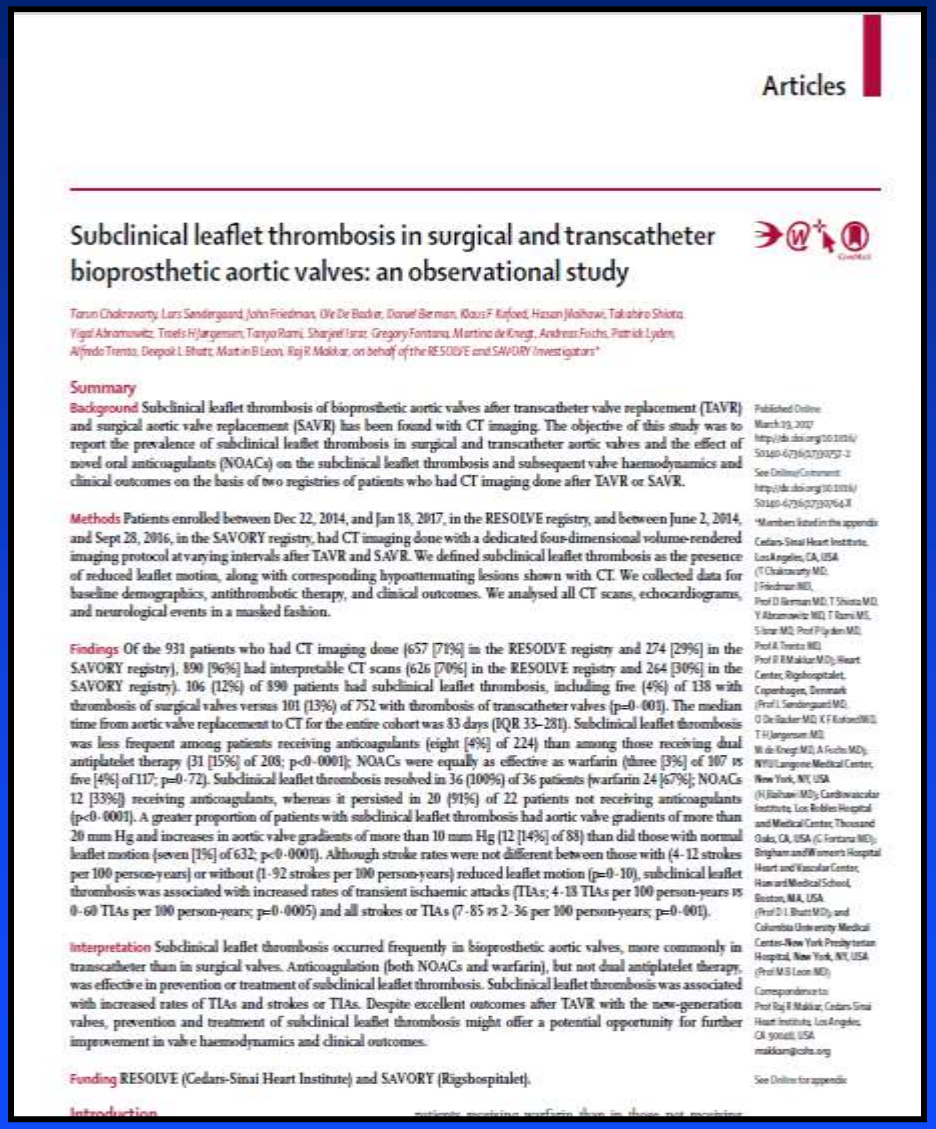
Freedom from THV degeneration



# at risk	378	199	116	43	7

THV degeneration was defined as at least moderate regurgitation AND/OR mean gradient ≥ 20mmHg, which did not appear within 30 days of the procedure and is not related to endocarditis.

Valve Thrombosis



Articles

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

Tarun Chakravarty, Lars Søndergaard, John Friedman, Ole De Backer, Daniel Berman, Klaus F Kofoed, Hasan Jilaihawi, Takahiro Shiota, Yigal Abramowitz, Troels H Jørgensen, Tanya Rami, Sharjeel Israr, Gregory Fontana, Martino de Knegt, Andreas Fuchs, Patrick Lyden, Alfredo Trento, Deepak L Bhatt, Martin B Leon, Raj R Makkar, on behalf of the RESOLVE and SAVORY Investigators*

Summary

Background Subclinical leaflet thrombosis of bioprosthetic aortic valves after transcatheter valve replacement (TAVR) and surgical aortic valve replacement (SAVR) has been found with CT imaging. The objective of this study was to report the prevalence of subclinical leaflet thrombosis in surgical and transcatheter aortic valves and the effect of novel oral anticoagulants (NOACs) on the subclinical leaflet thrombosis and subsequent valve haemodynamics and clinical outcomes on the basis of two registries of patients who had CT imaging done after TAVR or SAVR.

Methods Patients enrolled between Dec 22, 2014, and Jan 18, 2017, in the RESOLVE registry, and between June 2, 2014, and Sept 28, 2016, in the SAVORY registry, had CT imaging done with a dedicated four-dimensional volume-rendered imaging protocol at varying intervals after TAVR and SAVR. We defined subclinical leaflet thrombosis as the presence of reduced leaflet motion, along with corresponding hypoattenuating lesions shown with CT. We collected data for baseline demographics, antithrombotic therapy, and clinical outcomes. We analysed all CT scans, echocardiograms, and neurological events in a masked fashion.

Findings Of the 931 patients who had CT imaging done (657 [71%] in the RESOLVE registry and 274 [29%] in the SAVORY registry), 890 [96%] had interpretable CT scans (626 [70%] in the RESOLVE registry and 264 [30%] in the SAVORY registry). 106 (12%) of 890 patients had subclinical leaflet thrombosis, including five (4%) of 138 with thrombosis of surgical valves versus 101 (13%) of 752 with thrombosis of transcatheter valves (p=0·001). The median time from aortic valve replacement to CT for the entire cohort was 83 days (IQR 33–281). Subclinical leaflet thrombosis was less frequent among patients receiving anticoagulants (eight [4%] of 224) than among those receiving dual antiplatelet therapy (31 [15%] of 208; p<0·0001); NOACs were equally as effective as warfarin (three [3%] of 107 vs five [4%] of 117; p=0·72). Subclinical leaflet thrombosis resolved in 36 (100%) of 36 patients (warfarin 24 [67%]; NOACs 12 [33%]) receiving anticoagulants, whereas it persisted in 20 (91%) of 22 patients not receiving anticoagulants (p<0·0001). A greater proportion of patients with subclinical leaflet thrombosis had aortic valve gradients of more than 20 mm Hg and increases in aortic valve gradients of more than 10 mm Hg (12 [14%] of 88) than did those with normal leaflet motion (seven [1%] of 632; p<0·0001). Although stroke rates were not different between those with (4·12 strokes per 100 person-years) or without (1·92 strokes per 100 person-years) reduced leaflet motion (p=0·10), subclinical leaflet thrombosis was associated with increased rates of transient ischaemic attacks (TIAs; 4·18 TIAs per 100 person-years vs 0·60 TIAs per 100 person-years; p=0·0005) and all strokes or TIAs (7·85 vs 2·36 per 100 person-years; p=0·001).

Interpretation Subclinical leaflet thrombosis occurred frequently in bioprosthetic aortic valves, more commonly in transcatheter than in surgical valves. Anticoagulation (both NOACs and warfarin), but not dual antiplatelet therapy, was effective in prevention or treatment of subclinical leaflet thrombosis. Subclinical leaflet thrombosis was associated with increased rates of TIAs and strokes or TIAs. Despite excellent outcomes after TAVR with the new-generation valves, prevention and treatment of subclinical leaflet thrombosis might offer a potential opportunity for further improvement in valve haemodynamics and clinical outcomes.

Funding RESOLVE (Cedars-Sinai Heart Institute) and SAVORY (Rigshospitalet).

Published Online March 29, 2017 http://dx.doi.org/10.1016/S0140-6736(17)30957-2

See Online/Comment http://dx.doi.org/10.1016/S0140-6736(17)30964-X

*Members listed in the appendix

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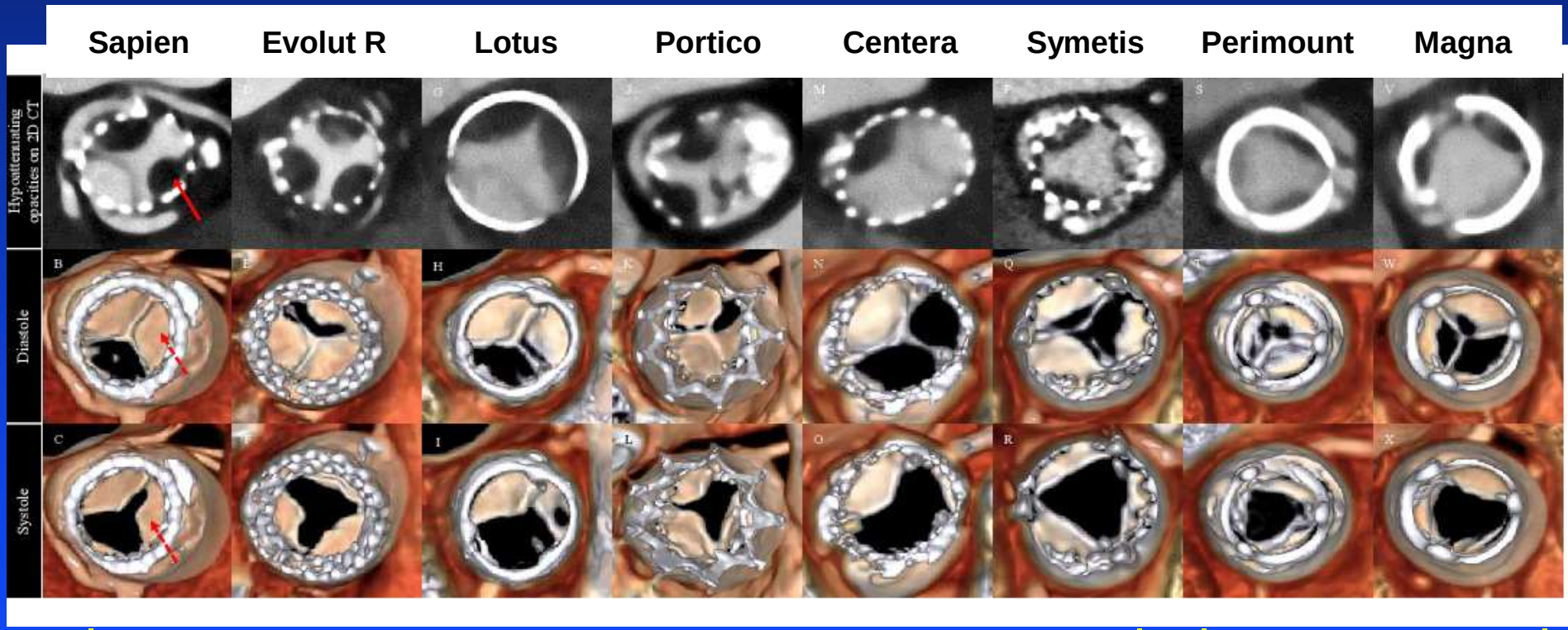
Correspondence to: Prof Raj R Makkar, Cedars-Sinai Heart Institute, Los Angeles, CA 90048, USA makkarr@cshs.org

See Online for appendix

Introduction

- 931 pts treated with either TAVR (n=752) or SAVR (n=138) who underwent CT imaging at 2 centers
- Median time to CT
  - *TAVR 58 days (IQR 32-236)*
  - *SAVR 162 days (IQR 79-417)*
- Valve thrombosis identified based on <u>hypoattenuated leaflet thickening</u> (on 3D CT) <u>and reduced leaflet motion (by 4D CT)</u>

Reduced leaflet motion seen in multiple valve types



TAVR

SAVR

Chakravarty T, et al. Lancet 2017

Key Findings

- Leaflet thrombosis was common (12% overall)→ more common with TAVR than SAVR (13% vs. 4%, =0.04)
- Leaflet thrombosis was generally subclinical, although it was associated with elevated transvalvular gradients in 14% of patients
- Thrombosis was less common among patients receiving oral anticoagulation than antiplatelet therapy (4% vs. 15%)
  - *Vitamin K antagonists and DOACs seemed to provide similar protection (4% vs. 3%)*
  - *DAPT no better than SAPT (14.9% vs. 15.6%)*
  - *Treatment with anticoagulants led to resolution of thrombosis in 36/36 cases (compared with just 2/22 with DAPT*

Chakravarty T, et al. Lancet 2017

Summary: Valve Thrombosis and Durability

- Reduced leaflet mobility almost certainly represents subclinical valve thrombosis
  - *Should have high degree of suspicion in patients who present with embolic phenomena (stroke, TIA) or unexplained increase in gradient*
  - *Unclear whether this is more of a problem with TAVR than SAVR given marked differences in patient populations in the observational study*
  - *Suggests the need for dedicated RCTs to identify the optimal anticoagulation regimen (and duration) after TAVR*
- Late valve degeneration after TAVR of uncertain significance
  - *RCTs vs. surgery in high risk patients have not suggested any differences in valve deterioration through 5 years*
  - *With increasing treatment of intermediate and low-risk patients, however, careful follow-up of both valve types using uniform definitions is essential*