New York Transcatheter Valves 2018

PATIENT FOCUSED EVIDENCE-BASED APPROACH

Role of Embolic Protection Devices in TAVR: Are They Needed? Waste of Time and Money?

Gian Paolo Ussia

Campus Bio-medico University, Rome Italy

g.ussia@unicampus.it

REQUIRED

Gian Paolo Ussia

I have no relevant financial relationships

Stroke After Transcatheter Aortic Valve Replacement: Incidence, Risk Factors, Prognosis, and Preventive Strategies

Ioannis Mastoris, MD; Mikkel M. Schoos, MD, PhD; George D. Dangas, MD, PhD; Roxana Mehran, MD
The Zena and Michael A. Wiener Cardiovascular Institute, the Icahn School of Medicine at Mount Sinai, New York, New York

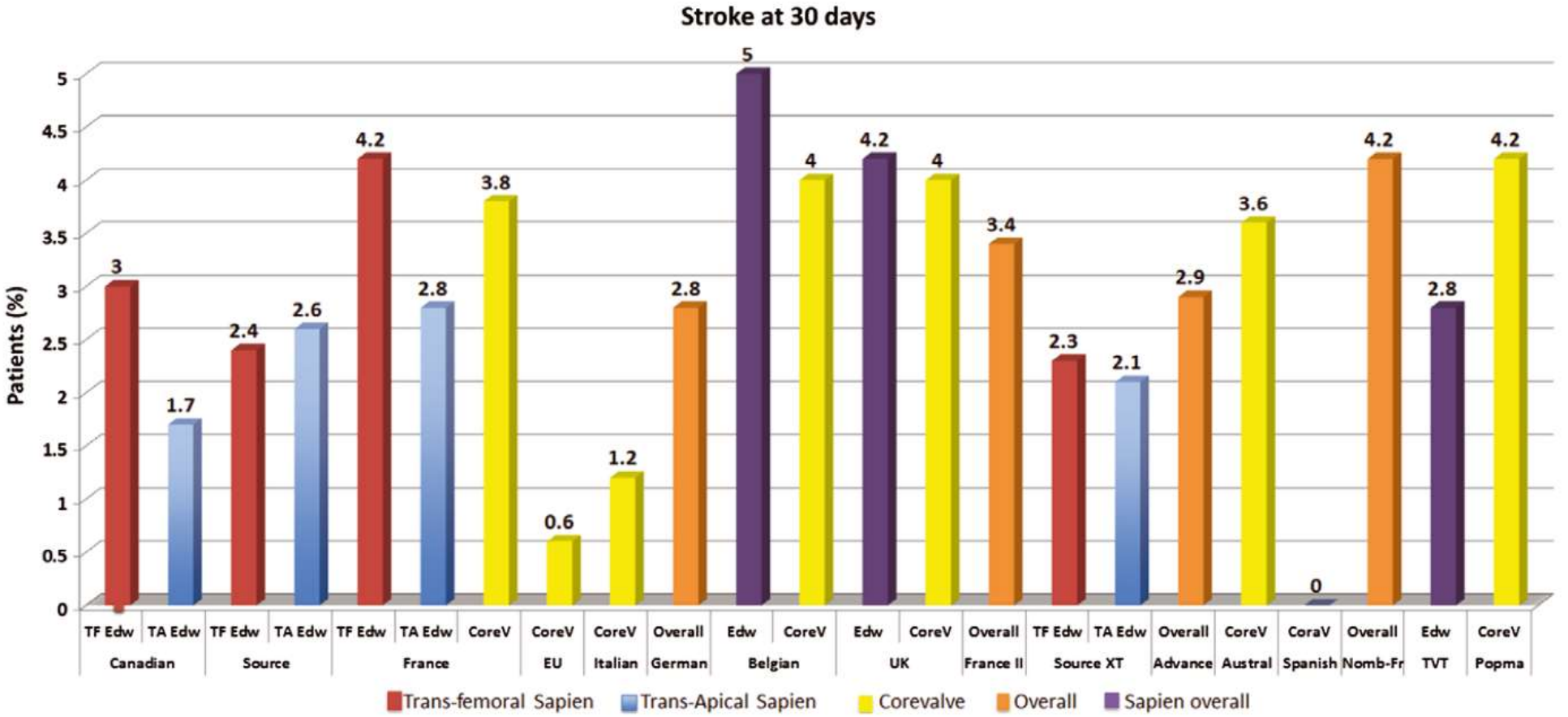
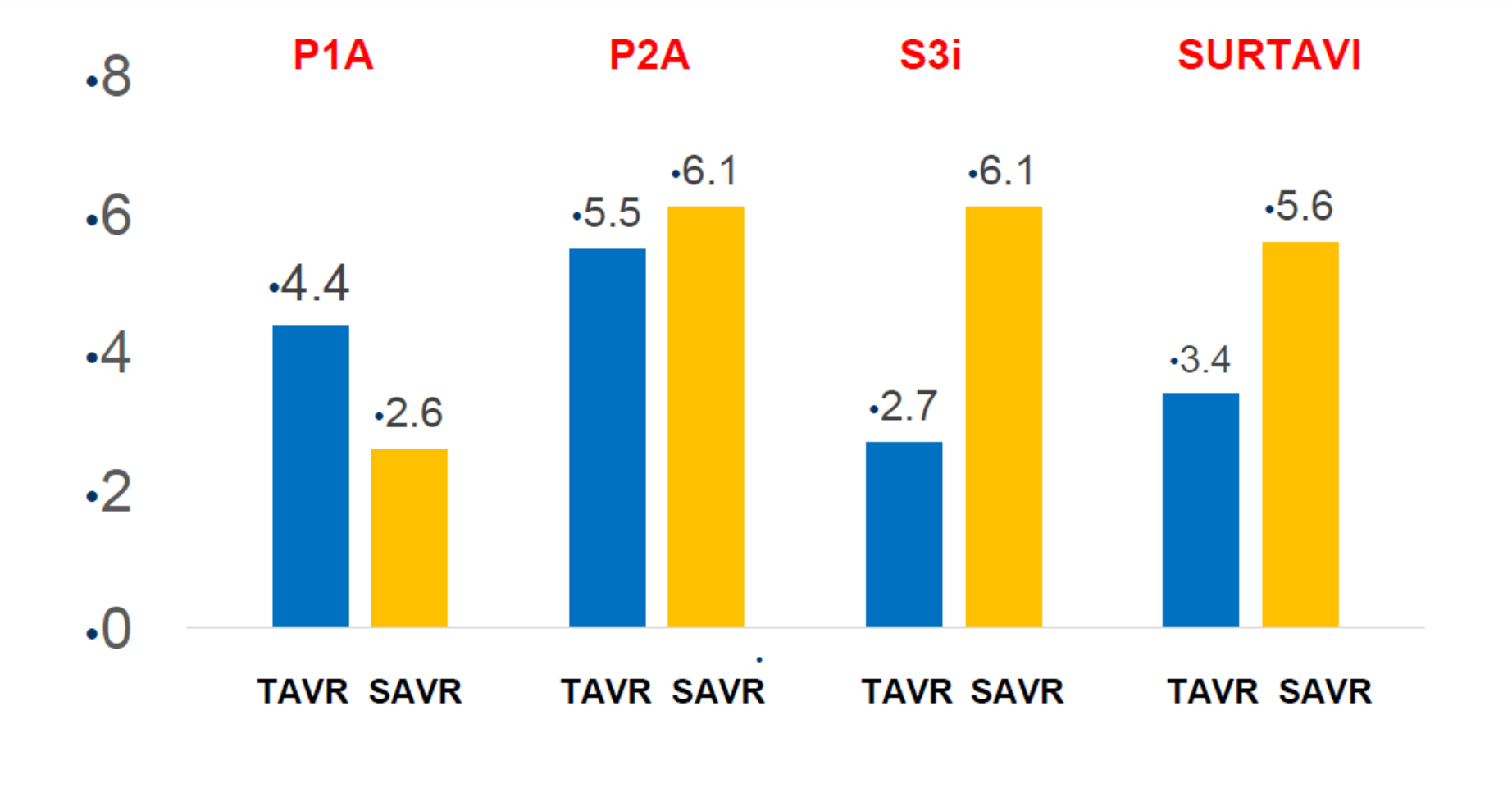


Figure 1. Registry-based incidence of major and minor stroke after TAVR in current clinical practice. Abbreviations: ACC, American College of Cardiology; TAVR, transcatheter aortic valve replacement; TVT, TransValvular Therapy registry. Data are from Rodes-Cabau et al.,[6] Thomas et al.,[7] Eltchaninoff et al.,[8] Piazza et al.,[9] Tamburino et al.,[41] Zahn et al.,[10] Bosmans et al.,[11] Moat et al,[12] Gilard et al.,[13] Avanzas et al.,[14] Nombela-Franco et al.,[36] Mack et al.,[57] Popma et al.[21]

Stroke randomized trial TAVR/SAVR



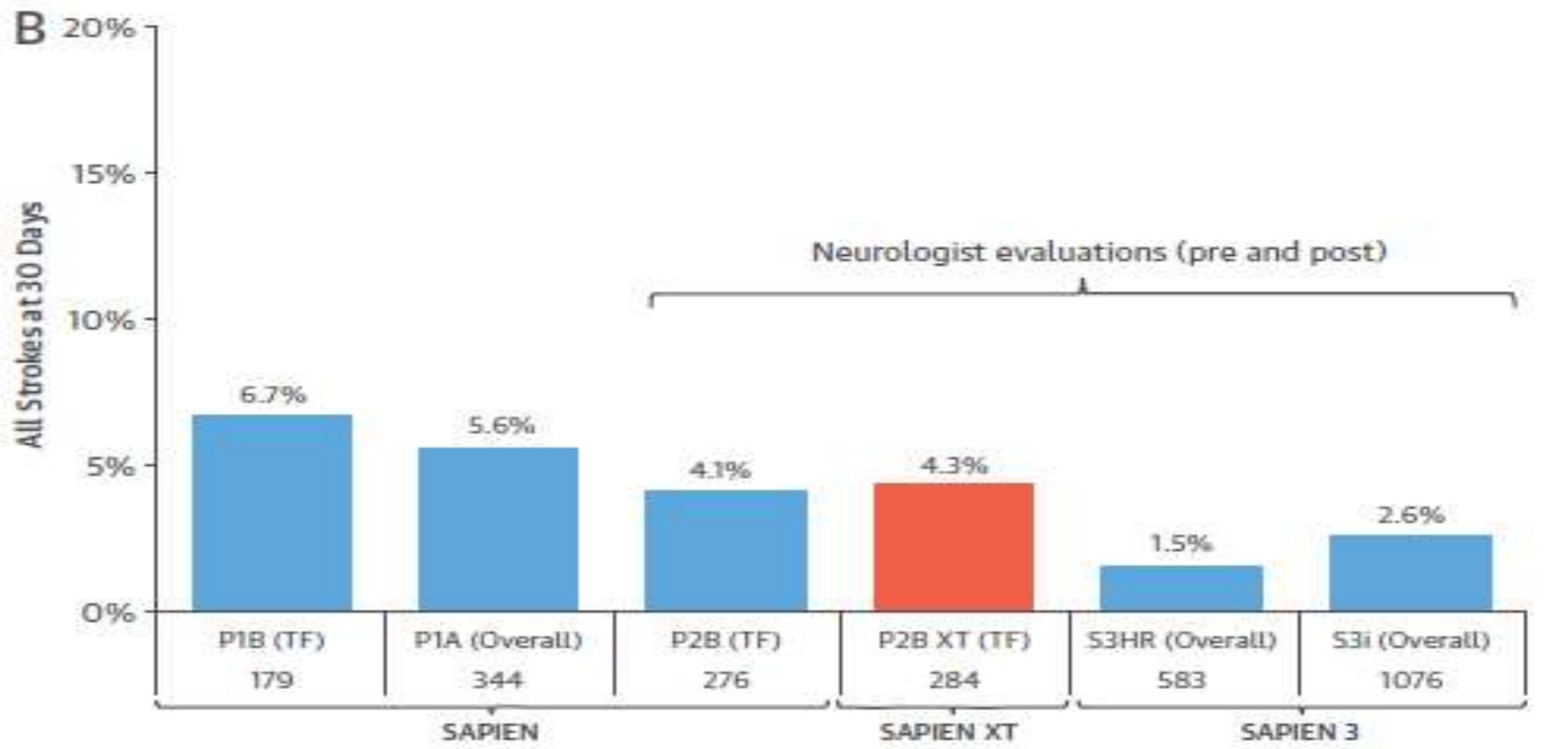
Stroke ↓

STATE-OF-THE-ART REVIEW

Transcatheter Aortic Valve Replacement 2016

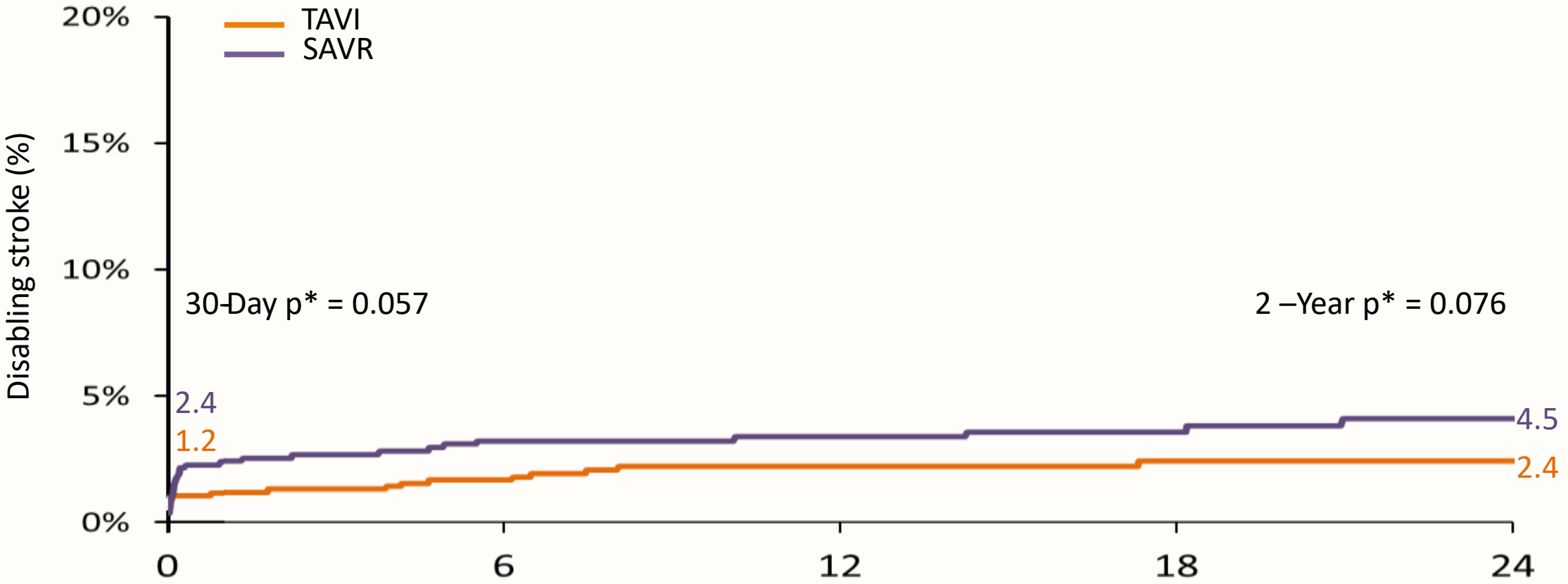
A Modern-Day "Through the Looking-Glass" Adventure

Torsten P. Vahl, MD, Susheel K. Kodali, MD, Martin B. Leon, MD



SURTAVI TRIAL

Incidence of disabling stroke

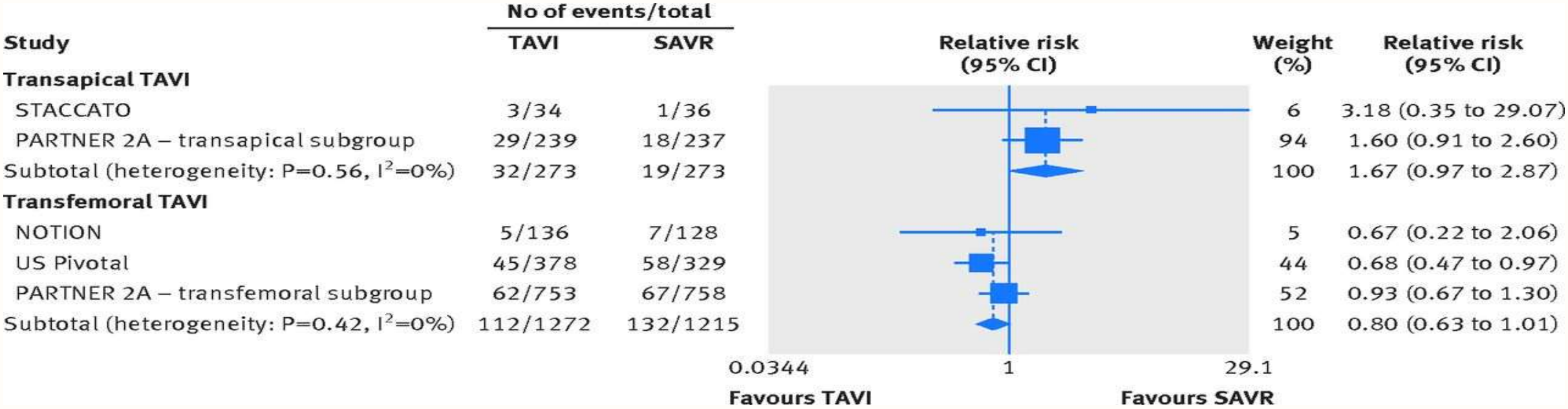


No. at Risk

TAVI	864	755	612	456	272
SAVR	796	674	555	407	241

* log-rank

Fig 4 Forest plot for relative risk of stroke at longest follow-up for transcatheter aortic valve implantation (TAVI) compared with surgical aortic valve replacement (SAVR) for severe aortic stenosis, by valve approach.



Reed A Siemieniuk et al. BMJ 2016;354:bmj.i5130

Stroke After Transcatheter Aortic Valve Replacement: Incidence, Risk Factors Prognosis, and Preventive Strategies

Ioannis Mastoris, MD; Mikkel M. Schoos, MD, PhD; George D. Dangas, Roxana Mehran, MD
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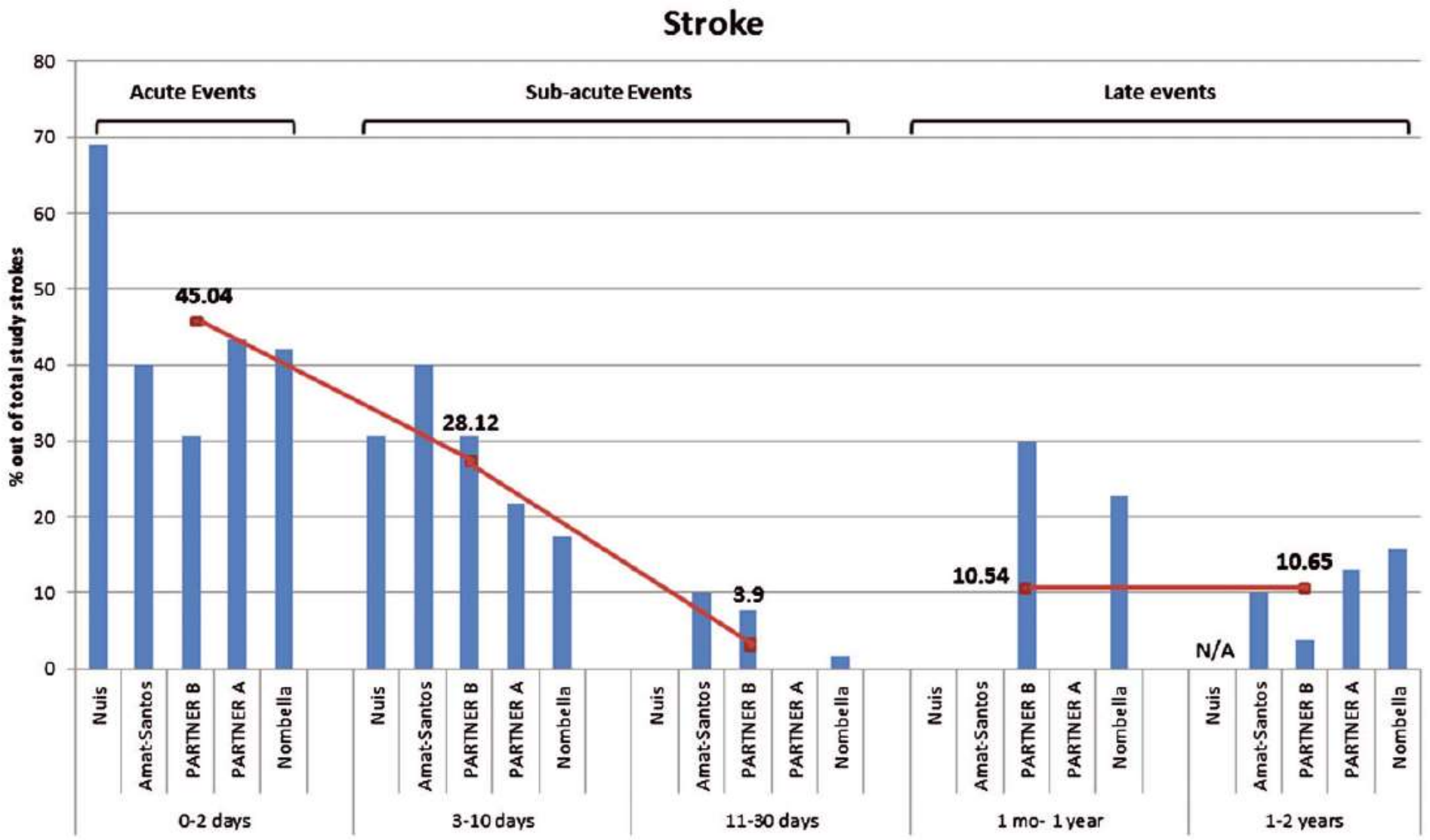


Figure 2. Timing of stroke after TAVR with approximately 2 years follow-up. Each bar-chart represents the percentage of strokes out of the total individual study strokes. Abbreviations: PARTNER, Placement of Aortic Transcatheter Valves; TAVR, transcatheter aortic valve replacement. Data are from Amat-Santos et al,[34] Nuis et al,[35] PARTNER A[3] and B,[17] and Nombela-Franco et al.[36]

Cerebral Embolic Protection During Transcatheter Aortic Valve Replacement

A Disconnect Between Logic and Data?*

Azeem Latib, MD,[a,b] Matteo Pagnesi, MD[a]

Silent Ischemia

- > 70% of TAVR have new silent cerebral lesions detected by post procedural diffusion-weighted magnetic resonance imaging (DW-MRI)
- Has been suggested that represent silent brain infarctions that could be related to memory loss, cognitive decline, and dementia
- One study showed a >2-fold risk of dementia and decline in cognitive function.
- The same association was found after cardiac surgery within 6 weeks after the procedure
- Another study showed that in pts with silent lesions 91% of them had preserved cognitive function at 2 years follow up and only 5.4% had early cognitive decline

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Table 3. Clinically Silent Cerebral Embolism Assessed With DW-MRI: Summary of Studies Available

Study	% of Patients With New Cerebral Lesions (n)			Mean No. of Infarcts Per Patient			Mean Lesion Volume and SD, cm^3		Mean Total Volume and SD, cm^3
	All	TF	TA	All	TF	TA	TF	TA	
Fairbairn et al, 2012[29]	77% (24/31)	77% (24/31)			4.2 ± 6.5				2.05 ± 3.5
Kahlert et al, 2010[18]	84.4% (27/32)	84.4% (27/32)			4.0 (2.1–6.0)		0.081 (0.06–0.10)		0.32
Ghanem et al, 2010[61]	72.7% (16/22)	72.7% (16/22)			3.4 ± 5.1				4.3 ± 14.9
Astarci et al, 2010[62]	91.5% (32/35)	90% (19/21)	93% (13/14)		5.9 ± 6.8	6.6 ± 7.1	0.475	2.170	2.
Rodés-Cabau et al, 2011[19]	68% (41/60)	66% (19/29)	71% (22/31)	3 (2–8)	3 (1–7)	4 (2–9)			
Average estimate	78.2%				4.1				2.4 ± 9.2

Abbreviations: DW-MRI, diffusion-weighted magnetic resonance imaging; SD, standard deviation; TA, transapical; TF, transfemoral.

Stroke After Transcatheter Aortic Valve Replacement: Incidence, Risk Factors, Prognosis, and Preventive Strategies

Ioannis Mastoris, MD; Mikkel M. Schoos, MD, PhD; George D. Dangas, MD, PhD; Roxana Mehran, MD
The Zena and Michael A. Wiener Cardiovascular Institute, the Icahn School of Medicine at Mount Sinai, New York, New York

Pathophysiology

- Stroke at 24h and 30 days strongly correlated to the procedure
- Retrograde crossing of a stenotic aortic valve results in new focal cerebral lesions in 22% of pts
- BAV could cause embolism of calcium deposits and increases the risk of thrombogenic complication
- The interaction of the stent valve with the aortic annulus over the displaced natural valve can cause additional embolic debris.
- Hypoperfusion may occur during BAV and balloon-expandable valve deployment due to repeated rapid ventricular pacing, results in transiently reduced cardiac output. This can induce ischemia in addition to impaire decreased washout of dislodged microemboli.
- prosthetic valve surface exposure, flow turbulence, blood stasis in the perivalvular space ‘‘outside’’ the metallic stent generate thrombi with subsequent events.

Van Mieghem Circulation 2013, Rodes Cabau JACC 2011, Popma JACC 2014, Stirtecky circulation 2012 Marechau EJCTS 2012, Kalhert Circulation 2012

Insights Into Timing, Risk Factors, and Outcomes of Stroke and Transient Ischemic Attack After Transcatheter Aortic Valve Replacement in the PARTNER Trial (Placement of Aortic Transcatheter Valves)

Samir Kapadia, MD; Shikhar Agarwal, MD; D. Craig Miller, MD; John G. Webb, MD; Michael Mack, MD; Stephen Ellis, MD; Howard C. Herrmann, MD; Augusto D. Pichard, MD; E. Murat Tuzcu, MD; Lars G. Svensson, MD, PhD; Craig R. Smith, MD; Jeevanantham Rajeswaran, PhD; John Ehrlinger, PhD; Susheel Kodali, MD; Raj Makkar, MD; Vinod H. Thourani, MD; Eugene H. Blackstone, MD; Martin B. Leon, MD

"...Improvements in the TAVR procedure may decrease risk of post-TAVR stroke. We observed that longer procedure time and more pacing runs and postdilatations were associated with a higher risk of stroke after TAVR (with variable reliability). Advances in valve and delivery-system design, alongwith increasing experience, may reduce procedure times and,thereby, reduce occurrence of stroke..."

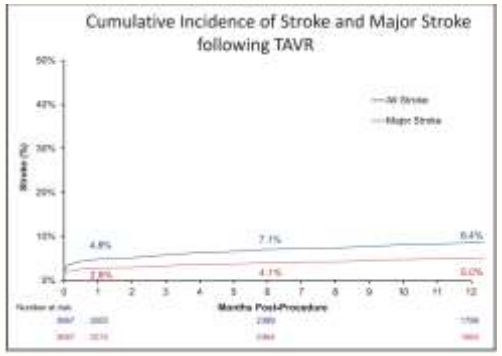
Table 3. Incremental Risk Factors for Stroke After Transcatheter Aortic Valve Replacement

Risk Factor	Coefficient±SE	*P* Value	Reliability, %*
TF-TAVR			
Early hazard phase			
Higher pre-TAVR aortic valve peak gradient†	0.33±0.16	0.04	62
Late hazard phase			
Dementia	1.2±0.48	0.01	82
Smaller prosthetic valve size: 23 mm (vs 26 mm)	0.62±0.34	0.07	53
TA-TAVR			
Early hazard phase			
Pure aortic stenosis without regurgitation	0.77±0.39	0.05	55
More postdilatations‡	0.18±0.082	0.03	51
Late hazard phase			
Race other than white	1.7±0.57	0.003	73
Lower left ventricular ejection fraction§	0.82±0.40	0.04	57
Atrial fibrillation	1.5±0.48	0.002	75

Neurological Events Following Transcatheter Aortic Valve Replacement and Their Predictors

A Report From the CoreValve Trials

Neal S. Kleiman, MD; Brijeshwar J. Maini, MD; Michael J. Reardon, MD; John Conte, MD; Stanley Katz, MD; Vivek Rajagopal, MD; James Kauten, MD; Alan Hartman, MD; Raymond McKay, MD; Robert Hagberg, MD; Jian Huang, MD; Jeffrey Popma, MD; for the CoreValve Investigators



Multivariable procedural predictors

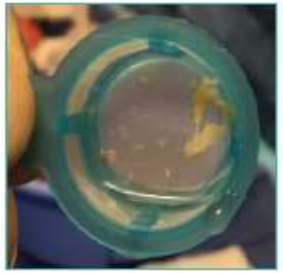
- total time in the cath lab or OR
- total delivery catheter time in the body
- rapid pacing during valvuloplasty
- repositioning of the CoreValve with a snare
- Number of valves implanted

Multivariable predictors

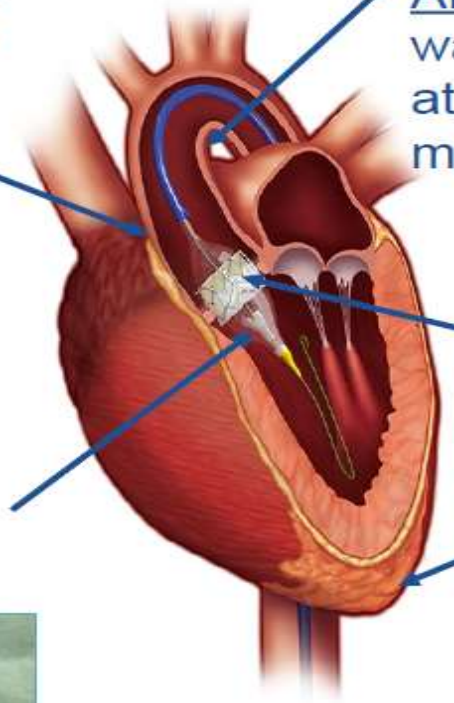
- total NIHSS score >0,
- Manifestations of prior CVA, prior TIA,
- peripheral vascular disease,
- absence of prior CABG
- presence of angina,
- low body mass index (<21 kg/m2),
- falls within the past 6 month

Sources of Debris During TAVR

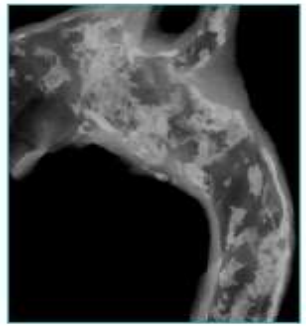
ASCENDING ARCH
Arterial wall, calcific and atherosclerotic material



STENOTIC VALVE
Leaflet tissue and calcific deposits



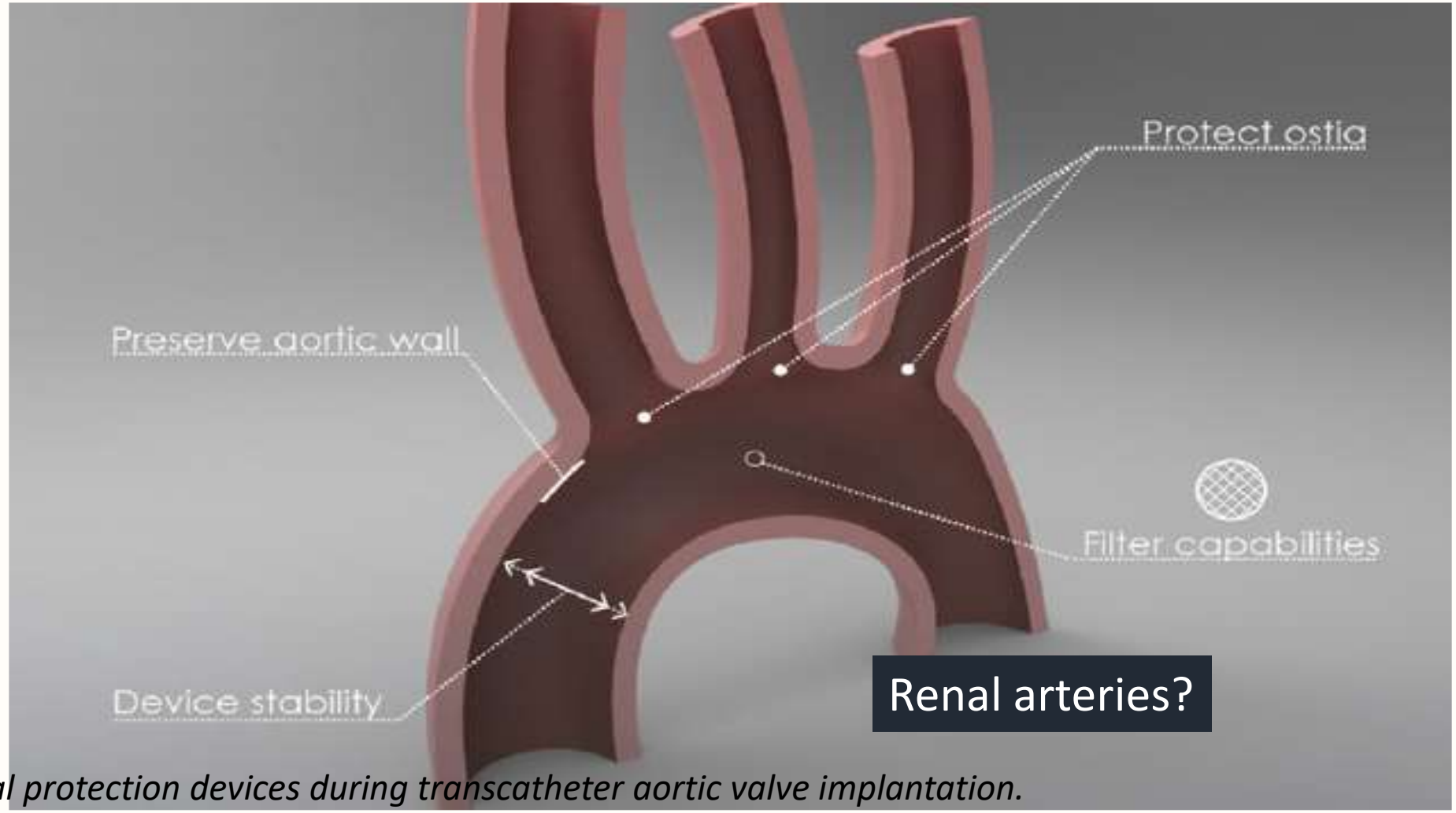
TRANSVERSE ARCH Arterial wall, calcific and atherosclerotic material



TAVR DEVICES
Foreign material

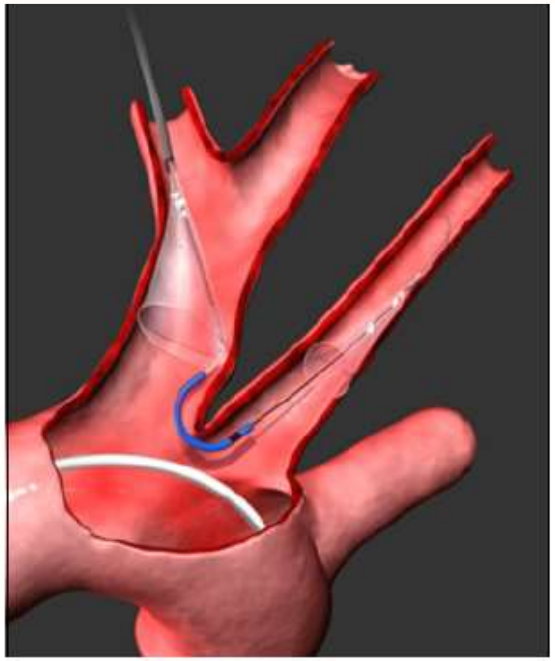
NATIVE HEART
Myocardium

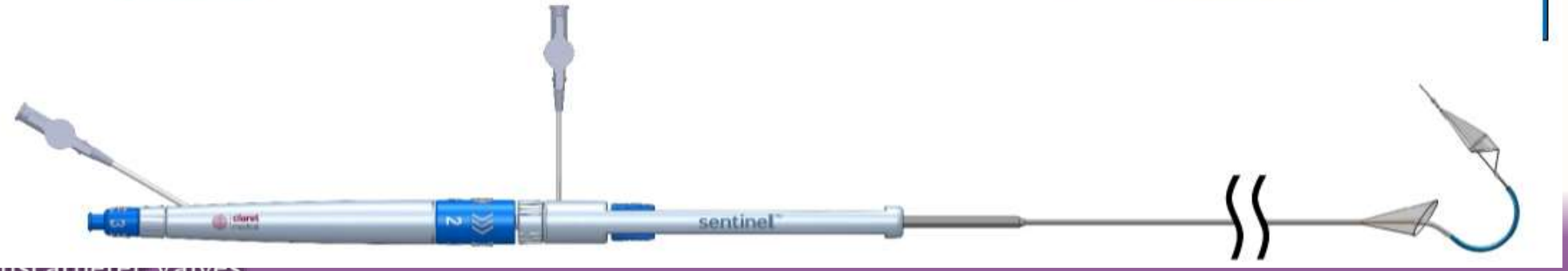
Mechanism of efficient Cerebral Embolic protection



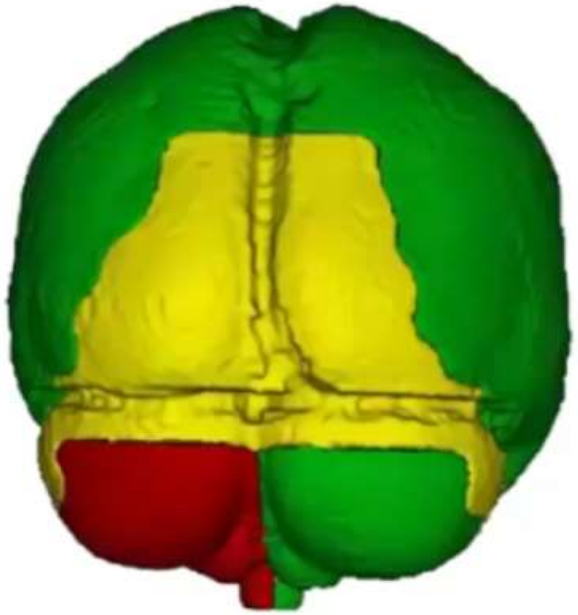
Wieneke Vlastra, et al. Cerebral protection devices during transcatheter aortic valve implantation. Trends in Cardiovasc Med 2018

Sentinel Embolic protection (Boston Scientific)

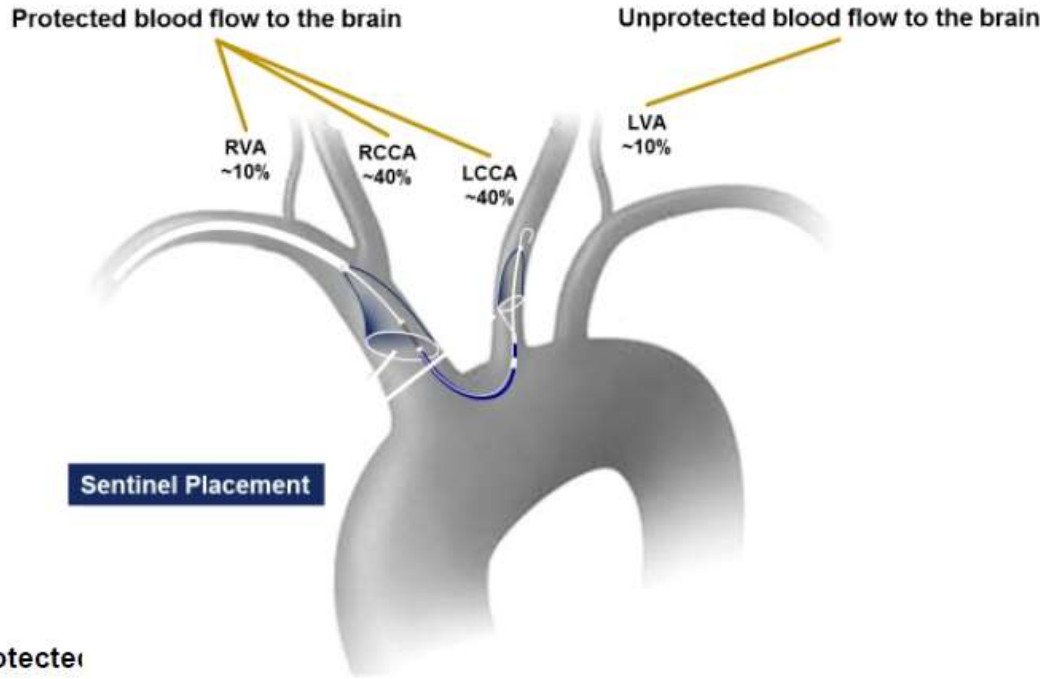




Sentinel Filters Protection

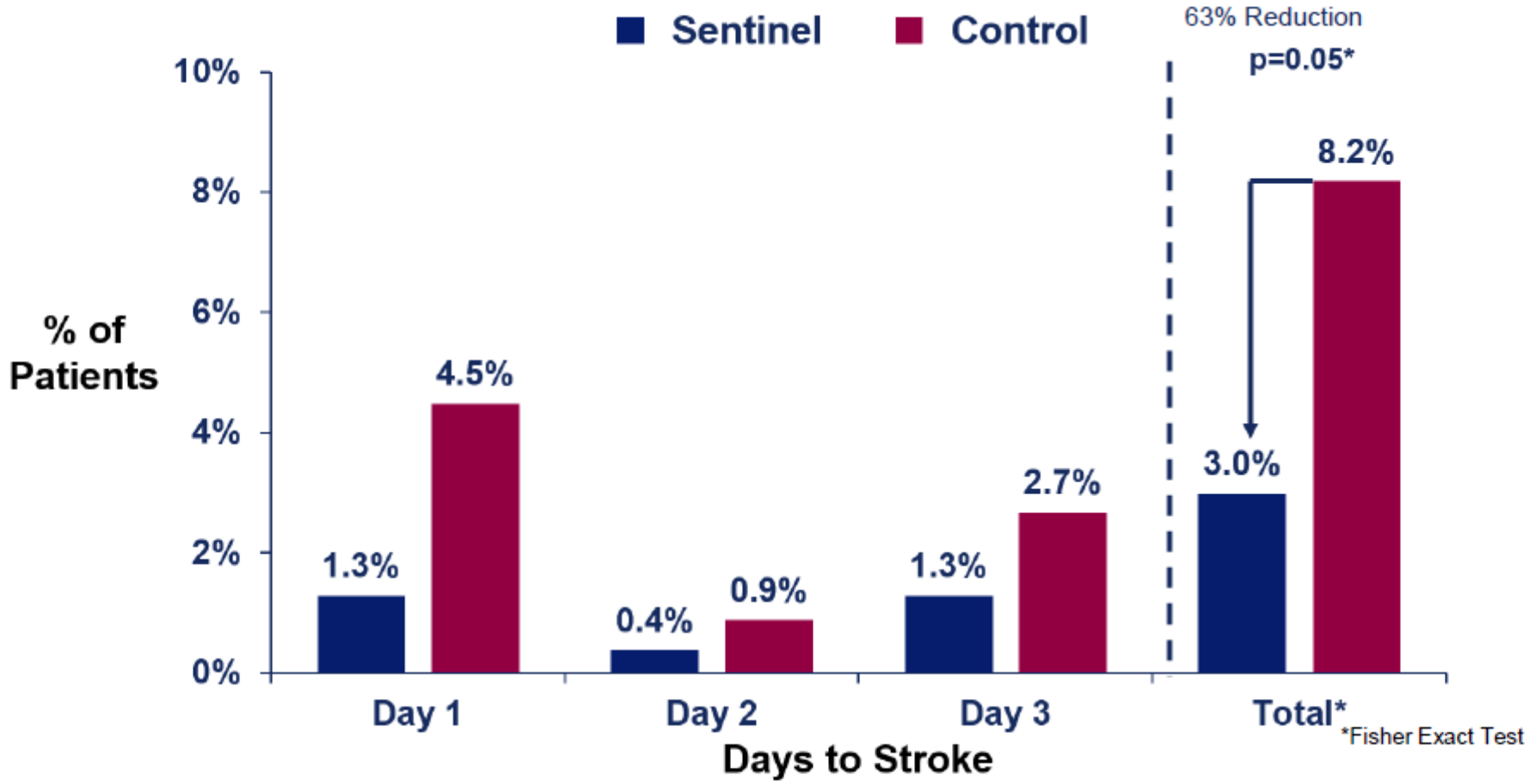


- Fully Protected
  - 74% brain volume
- Partially Protected
  - 24% brain volume
- Unprotecte
  - 2% brain volume



Zhao M, et al. Regional Cerebral Blood Flow Using Quantitative MR Angiography. *AJNR* 2007;28:1470-1473

Stroke reduction with CPF



95% of SENTINEL patients were evaluated by neurologists
Clinical Events Committee included 2 stroke neurologists

SENTINEL trial. Data presented at Sentinel FDA Advisory Panel, February 23, 2017

Kapadia SR et al. JACC 2017

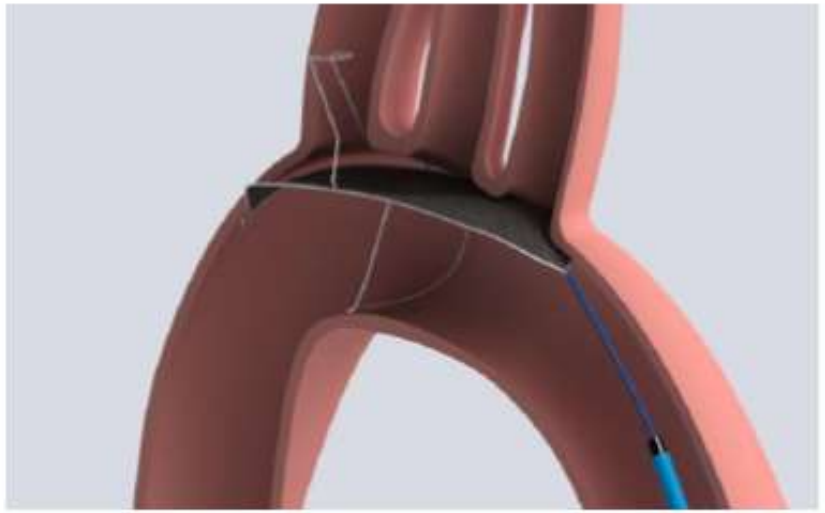
Registries

Study Center • Total N • Timing	Unprotected TAVR Patients Neurological Event Rate % (n/N)	Sentinel TAVR Patients Neurological Event Rate % (n/N)	Relative Risk Reduction (RRR)	Number-needed-to-treat (NNT) to avoid one event	Specific Measures
Ulm University[1] • N=560 • May 2017	4.6% (13/280)	1.4% (4/280)	70%	22	Propensity-score-matched All-stroke at 7-days
Pinnacle Health[2] • N=122 • Feb 2018	10% (7/69)	0% (0/53)	100%	10	All-stroke at 7-days Length-of-stay (LOS) reduced from 3.2d without protection to 1.5d with Sentinel
Erasmus, Rotterdam[3] • N=747 • March 2018	5% (23/453)	1% (3/294)	80%	25	All-stroke + TIA at 3-days
	3.8% (17/453)	1% (3/294)	74%	36	All-stroke at 3-days
Cedars Sinai[4] • N=419 • March 2018	6.3% (8/128)	1.4% (4/291)	78%	21	All-stroke at 7-days

1. Seeger J, et al. JACC Cardiovasc Interv. 2017 Nov 27;10(22):2297-2303
2. Gada H, presented at CMS NTAP Town Hall meeting Feb 2018
3. Van Mieghem N, presented at JIM and CRT 2018, manuscript in preparation
4. Makkar R, presented at CRT 2018, manuscript in preparation

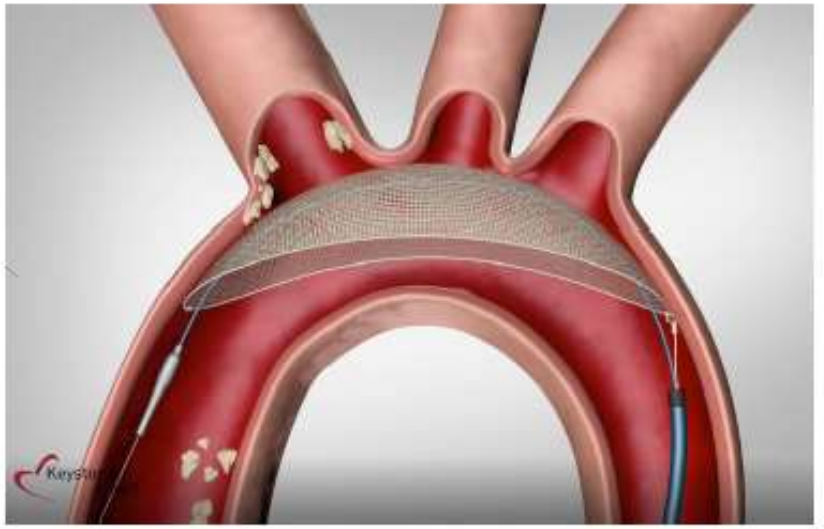
TriGuard HDH vs TriGUARD *3*

- ***TriGuard HDH***



- ***Nitinol frame with upper and lower stabilizers***
- ***Nitinol mesh (pore size 130x250 µm)***
- ***Filter area = 20.9 cm²***
- ***9 Fr RX delivery***

- ***TriGUARD 3***



- ***Self-positioning, nitinol frame without stabilizers***
- ***PEEK mesh (pore size 115x145 µm)***
- ***Filter area = 68.3 cm²***
- ***8 Fr OTW delivery***

REFLECT Trial Design (Phase I & II)

REFLECT

- Prospective, single-blind, randomized (2:1 device: control), multi-center safety & efficacy trial in two phases of the Keystone Heart Cerebral Embolic Protection Devices:
  - Phase 1 - TriGuard HDH
  - Phase 2 - TriGUARD *3*

- Study Chairman: Jeffrey Moses
- Study PI: Tamim Nazif
- Co-PIs: Alexandra Lansky
  - Raj Makkar
  - Andreas Baumbach
  - Joachim Schofer

TriGuard HDH

TriGUARD *3*

Metanalysis

Table 2 Clinical outcomes for TAVR with and without cerebral protection

Study	Author	Year	30-day stroke (%)		30-day mortality (%)		Life threatening bleed (%)		Acute kidney injury (%)		Major vascular complications (%)	
			TAVR + CP	TAVR	TAVR + CP	TAVR	TAVR + CP	TAVR	TAVR + CP	TAVR	TAVR + CP	TAVR
CLEAN-TAVI	Haussig *et al.*	2014	8.0	8.0	0.0	2.0	2.0	2.0	2.0	10.0	10.0	12.0
DEFLECT-III	Lansky *et al.*	2015	4.3	5.1	2.2	5.1	2.2	7.7	2.2	0.0	17.4	20.5
EMBOL-X	Wednt *et al.*	2015	0.0	0.0	0.0	0.0	NR	NR	NR	NR	NR	NR
MISTRAL-C	Van Mieghem *et al.*	2015	3.1	21.2	3.1	9.1	3.1	15.2	0.0	3.0	0.0	18.2
SENTINEL	Kapadia *et al.*	2017	5.6	9.1	1.3	1.8	NR	NR	0.4	0.0	8.6	5.9
Total	–	–	5.4	9.3	1.3	3.2	2.3	7.4	0.8	2.6	9.1	11.2

CP, cerebral protection; NR, not reported; TAVR, transcatheter aortic valve replacement.

J Thorac Dis 2018;10(3):1927-1935

Original Article

Cerebral protection devices in transcatheter aortic valve replacement: a clinical meta-analysis of randomized controlled trials

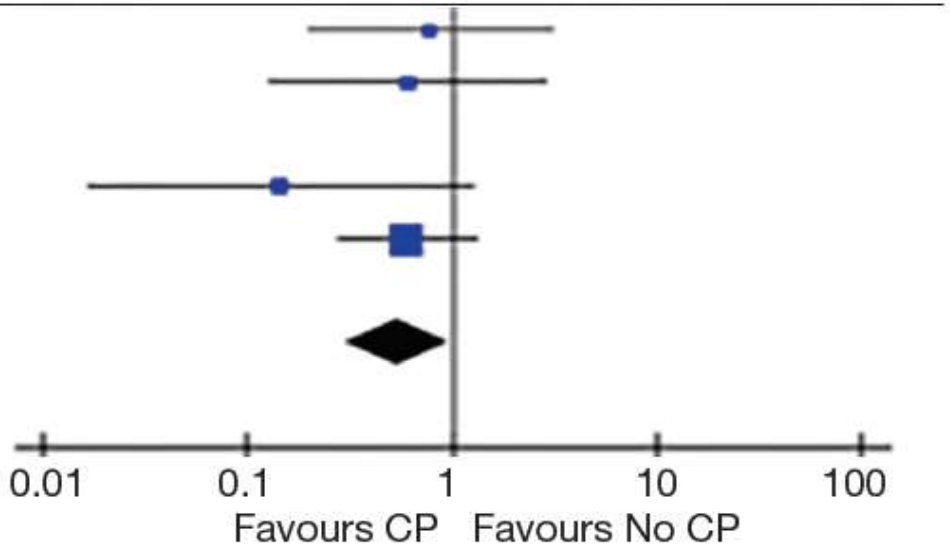
Nelson Wang, Kevin Phan

Combined stroke&mortality @ 30 days

A	CP		No CP			Odds Ratio
Study or subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
CLEAN-TAVI	4	50	5	50	15.6%	0.78 [0.20, 3.10]
DEFLECT-III	3	46	4	39	13.7%	0.61 [0.13, 2.91]
EMBOL-X	0	14	0	16		Not estimable
MISTRAL-C	1	32	6	33	19.4%	0.15 [0.02, 1.28]
SENTINEL	16	234	12	111	51.3%	0.61 [0.28, 1.33]
Total (95% CI)		376		249	100.0%	0.54 [0.30, 0.98]
Total events	24		27			

Heterogeneity: $Chi^2=1.77$, $df=3$ ($P=0.62$); $I^2=0\%$

Test for overall effect: $Z=2.03$ ($P=0.04$)



J Thorac Dis 2018;10(3):1927-1935

Cerebral replacement trials

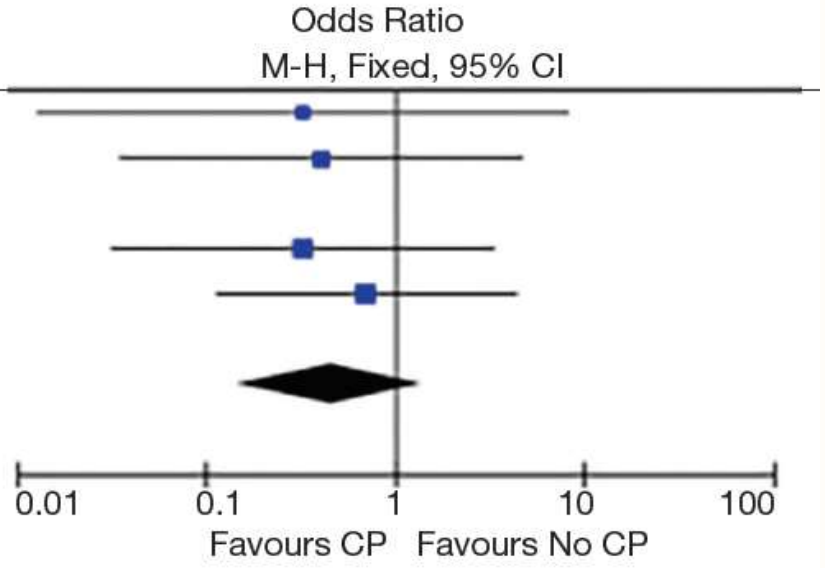
Nelson Wang, Kevi

Stroke @ 30 days

Study or subgroup	CP Events	CP Total	No CP Events	No CP Total	Weight	Odds Ratio M-H, Fixed, 95% CI
CLEAN-TAVI	0	50	1	50	16.2%	0.33 [0.01, 8.21]
DEFLECT-III	1	46	2	39	23.2%	0.41 [0.04, 4.71]
EMBOL-X	0	14	0	16		Not estimable
MISTRAL-C	1	32	3	33	31.3%	0.32 [0.03, 3.28]
SENTINEL	3	234	2	111	29.3%	0.71 [0.12, 4.30]
Total (95% CI)		376		249	100.0%	0.46 [0.15, 1.40]
Total events	5		8			

Heterogeneity: $Chi^2=0.36$, df=3 (P=0.95); $I^2=0\%$

Test for overall effect: Z=1.37 (P=0.17)

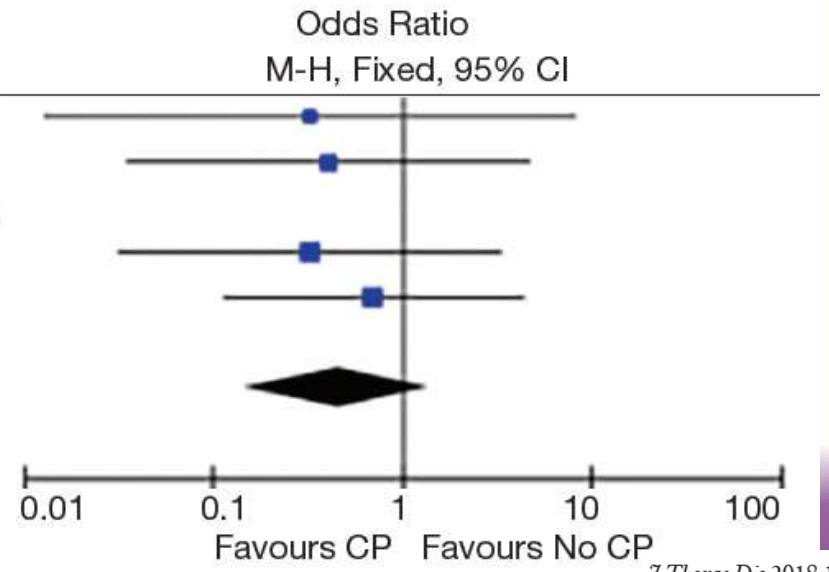


Mortality @ 30 days

Study or subgroup	CP Events	CP Total	No CP Events	No CP Total	Weight	Odds Ratio M-H, Fixed, 95% CI
CLEAN-TAVI	0	50	1	50	16.2%	0.33 [0.01, 8.21]
DEFLECT-III	1	46	2	39	23.2%	0.41 [0.04, 4.71]
EMBOL-X	0	14	0	16		Not estimable
MISTRAL-C	1	32	3	33	31.3%	0.32 [0.03, 3.28]
SENTINEL	3	234	2	111	29.3%	0.71 [0.12, 4.30]
Total (95% CI)		376		249	100.0%	0.46 [0.15, 1.40]
Total events	5		8			

Heterogeneity: $Chi^2=0.36$, df=3 (P=0.95); $I^2=0\%$

Test for overall effect: Z=1.37 (P=0.17)



Cerebral
replacer
trials

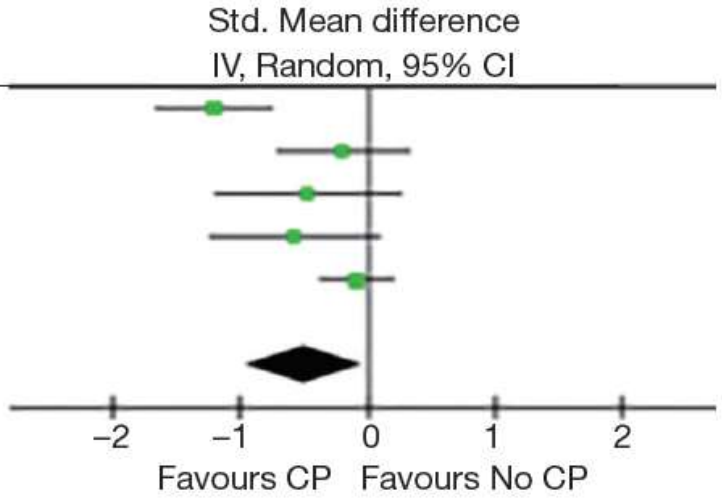
Nelson Wan

New total volume lesions @ 30 days

Study or subgroup	CP Mean	CP SD	CP Total	No CP Mean	No CP SD	No CP Total	Weight	Std. Mean difference IV, Random, 95% CI
CLEAN-TAVI	219.3	170.2	45	588.7	400	43	21.5%	−1.20 [−1.66, −0.75]
DEFLECT-III	58.5	52.5	33	68.3	43.8	26	20.3%	−0.20 [−0.71, 0.32]
EMBOL-X	88	60	14	168	217	16	16.3%	−0.47 [−1.20, 0.25]
MISTRAL-C	120.7	191.7	22	272.3	333.2	15	17.3%	−0.58 [−1.25, 0.10]
SENTINEL	383.2	538.2	91	425	562.4	98	24.6%	−0.08 [−0.36, 0.21]
Total (95% CI)			205			198	100.0%	−0.49 [−0.96, −0.03]

Heterogeneity: $Tau^2=0.21$; $Chi^2=17.71$, df=2 (P=0.94); $I^2=0\%$

Test for overall effect: Z=1.52 (P=0.13)

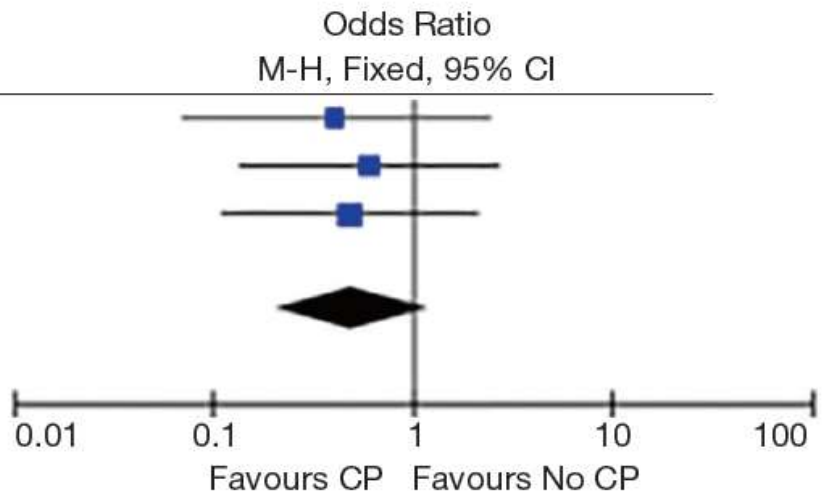


Pts with new brain lesions @ 30 days

Study or subgroup	CP Events	CP Total	No CP Events	No CP Total	Weight	Odds Ratio M-H, Fixed, 95% CI
DEFLECT-III	16	22	13	15	30.0%	0.41 [0.07, 2.38]
EMBOL-X	8	14	11	16	31.3%	0.61 [0.14, 2.71]
MISTRAL-C	26	33	23	26	38.8%	0.48 [0.11, 2.10]
Total (95% CI)		69		57	100.0%	0.50 [0.20, 1.23]
Total events	50		47			

Heterogeneity: $Chi^2=0.11$, df=2 (P=0.94); $I^2=0\%$

Test for overall effect: Z=1.52 (P=0.13)




Neurological Outcomes With Embolic Protection Devices in Patients Undergoing Transcatheter Aortic Valve Replacement

A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Gennaro Giustino, MD,[a] Roxana Mehran, MD,[b] Roland Veltkamp, MD,[c] Michela Faggioni, MD,[a] Usman Baber, MD,[a] George D. Dangas, MD, PhD[a]

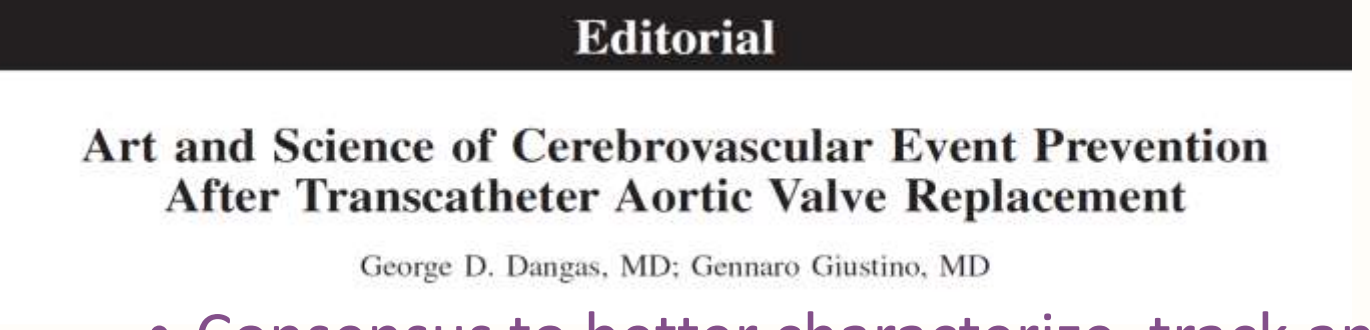
Considerations

- Metanalysis failed to detect a significant reduction in clinically overt stroke and all-cause mortality. However, both endpoints were numerically lower in the EP group.
- The effect of EP on neurological imaging endpoints appeared to be uniform between SE and BE valve types, which differ significantly in terms of design and implantation technique.
- Because a substantial number of emboli during TAVR are of thrombotic origin, complementary antithrombotic strategies to EP are warranted

Technical and procedural factors favouring CVA

- Thrombus formation in large diameter sheath despite optimal anticoagulation
- Wire and catheter manipulation in aortic arch,
- Aggressive retrograde aortic valve crossing
- Suboptimal preparatory BAV (ineffective RVP and eccessive balloon movement)
- DCS navigation
- ↓ cardiac output reduce cerebral perfusion which can results in diffuse silent ischemia
  - RV pacing during BAV pre and post implant or during valve implant
  - Hemodynamic instability

Device malpositioning, dislodgment, or embolization;


Editorial

Art and Science of Cerebrovascular Event Prevention After Transcatheter Aortic Valve Replacement

George D. Dangas, MD; Gennaro Giustino, MD

- Consensus to better characterize, track,and report CVEs in TAVR and SAVR
  - accuracy
  - etiology (stroke because of atrial fibrillation versus device thrombosis)
  - Easy of use (ex noncomplex tools in diagnosis)
- The importance of antithrombotic drugs in mitigating stroke risk after TAVR,
- Characterize modifiable factors for periprocedural stroke to identify patients who may benefit of intraprocedural embolic protection devices
  - complex anatomic characteristics (eg, highly calcified native valves, large aortic arc atheromas, or angulated aorta)
  - Aortic valve mobile vegetations
  - expected challenging-longer procedures.

Role of Embolic Protection Devices in TAVR: Are They Needed? Waste of Time and Money?

- Yes if is used extensively
- No if we are able to Identify patient at risk of intra-periprocedurale CVA:
- Optimize procedure technique
  - Be Precise, follow rigorously all the procedural steps, don’t waste time be fast but not in hurry
  - Reduce unuseful manipulation
    - aggressive approach for crossing the valve
    - mantain the wire in the ventricle,
    - reduce RV Pacing for BAV pre and post
    - during deployement mantain the valve position
- Use CEP in patient considered at high risk for CVA
- Avoid CEP if:
  - Unfavourable vascular anatomy
  - Potential device related complication of the procedure

Discussion

1. Who is the patient at higher risk of periprocedural stroke?
2. Do the younger or lower risk patient benefit more of the cerebral embolic protection?
3. Technical advise for reducing periprocedural stroke.
4. Concern about potential complication during CEP device manipulation/postioning?
5. Importance of full protection of epiaortic vessels.


Thank You