

Strokes After TAVR

Reasons for Declining Frequency

Samir Kapadia, MD
Professor of Medicine
Director, Cardiac Catheterization Laboratory
Cleveland Clinic

Disclosure

- **NONE**

EDITORIALS



Transcatheter Aortic-Valve Implantation — At What Price?

Hartzell V. Schaff, M.D.

In 2000, Bonhoeffer et al. described transvenous placement of a pulmonary-valve prosthesis and speculated that similar technology might be used in other cardiac valves, including the aortic position.³ Two years later, the first transcatheter insertion of an aortic-valve prosthesis was performed by Cribier et al.² Transcatheter aortic-valve

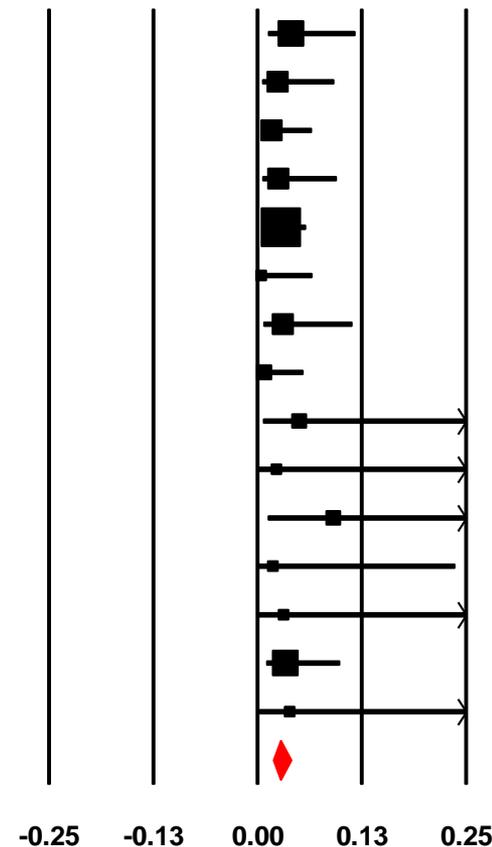
patients who are eligible for transfemoral insertion and may decrease vascular injury.

But the increased risk of stroke associated with transcatheter replacement, as compared with surgical replacement, is a special concern. Smith and colleagues report a 5.5% risk of stroke or transient ischemic attack within 30 days after

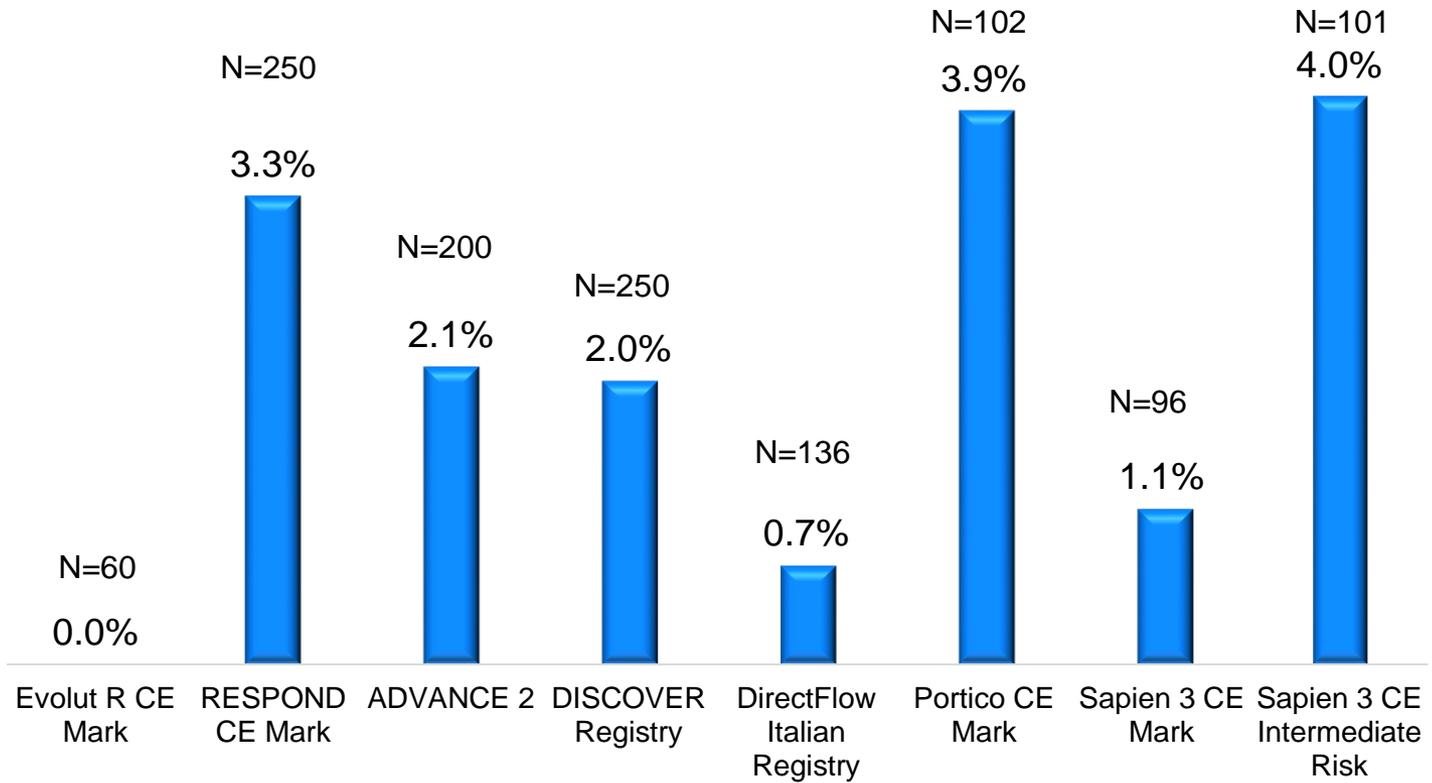
Second Generation Valves

Study name Outcome Statistics for each study Event rate and 95% CI

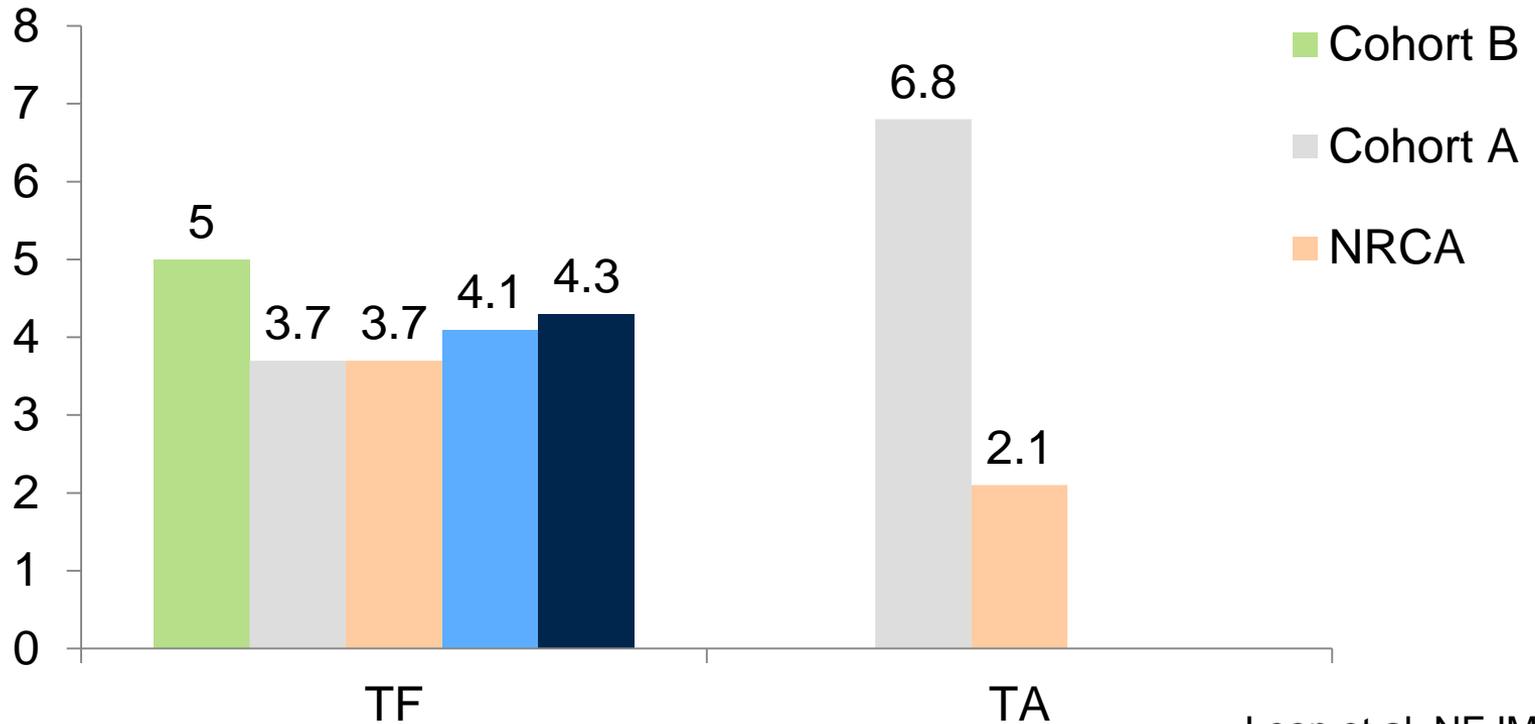
		Event rate	Lower limit	Upper limit	Z-Value	p-Value	Total
DFM (DISCOVER)	Major Stroke	0.040	0.013	0.117	-5.393	0.000	3 / 75
Portico (CE Trial)	Major Stroke	0.024	0.006	0.091	-5.171	0.000	2 / 83
Sadra Lotus (REPRISE)	Major Stroke	0.017	0.004	0.065	-5.706	0.000	2 / 119
ACURATE TF (CE Trial)	Major Stroke	0.025	0.006	0.094	-5.116	0.000	2 / 80
ACURATE TA (SAVI)	Major Stroke	0.028	0.013	0.058	-9.253	0.000	7 / 250
JenaValve (Jupiter)	Major Stroke	0.004	0.000	0.065	-3.840	0.000	0 / 115
JenaValve (CE mark)	Major Stroke	0.030	0.008	0.113	-4.826	0.000	2 / 66
ENGAGER (CE Trial)	Major Stroke	0.008	0.001	0.055	-4.801	0.000	1 / 125
DFM (Treede)	Major Stroke	0.050	0.007	0.282	-2.870	0.004	1 / 20
Portico (Manoharan)	Major Stroke	0.023	0.001	0.277	-2.629	0.009	0 / 21
Sadra Lotus (Meredith)	Major Stroke	0.091	0.013	0.439	-2.195	0.028	1 / 11
SAPIEN 3 (Dvir)	Major Stroke	0.019	0.001	0.236	-2.781	0.005	0 / 26
CENTERA (Binder)	Major Stroke	0.031	0.002	0.350	-2.390	0.017	0 / 15
ACURATE TA (Walther)	Major Stroke	0.033	0.011	0.098	-5.734	0.000	3 / 90
JenaValve (Mohr)	Major Stroke	0.038	0.002	0.403	-2.232	0.026	0 / 12
		0.028	0.019	0.040	-18.059	0.000	



Latest Stroke Data from Other Studies

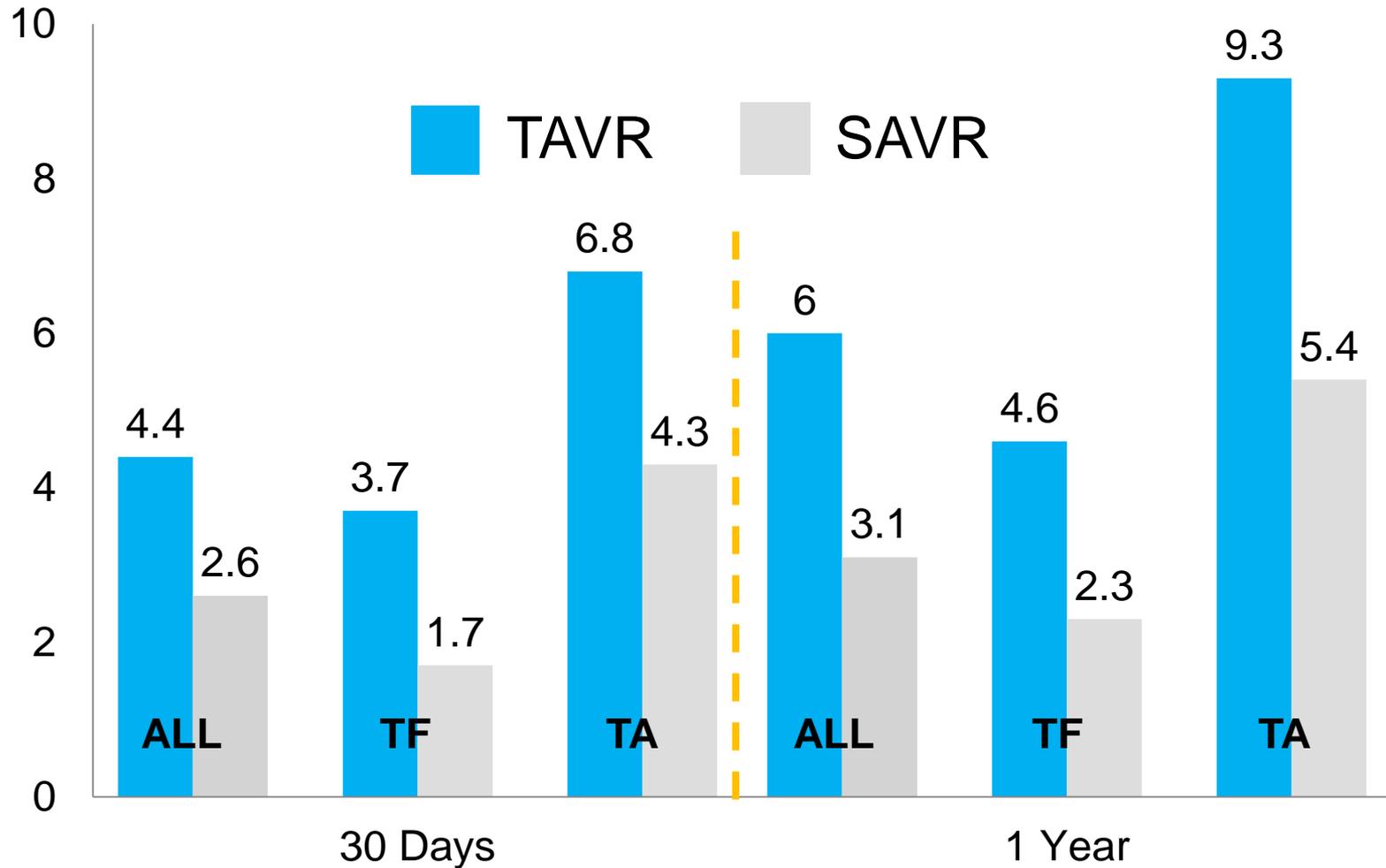


30 Days - All Stroke from PARTNER Trials

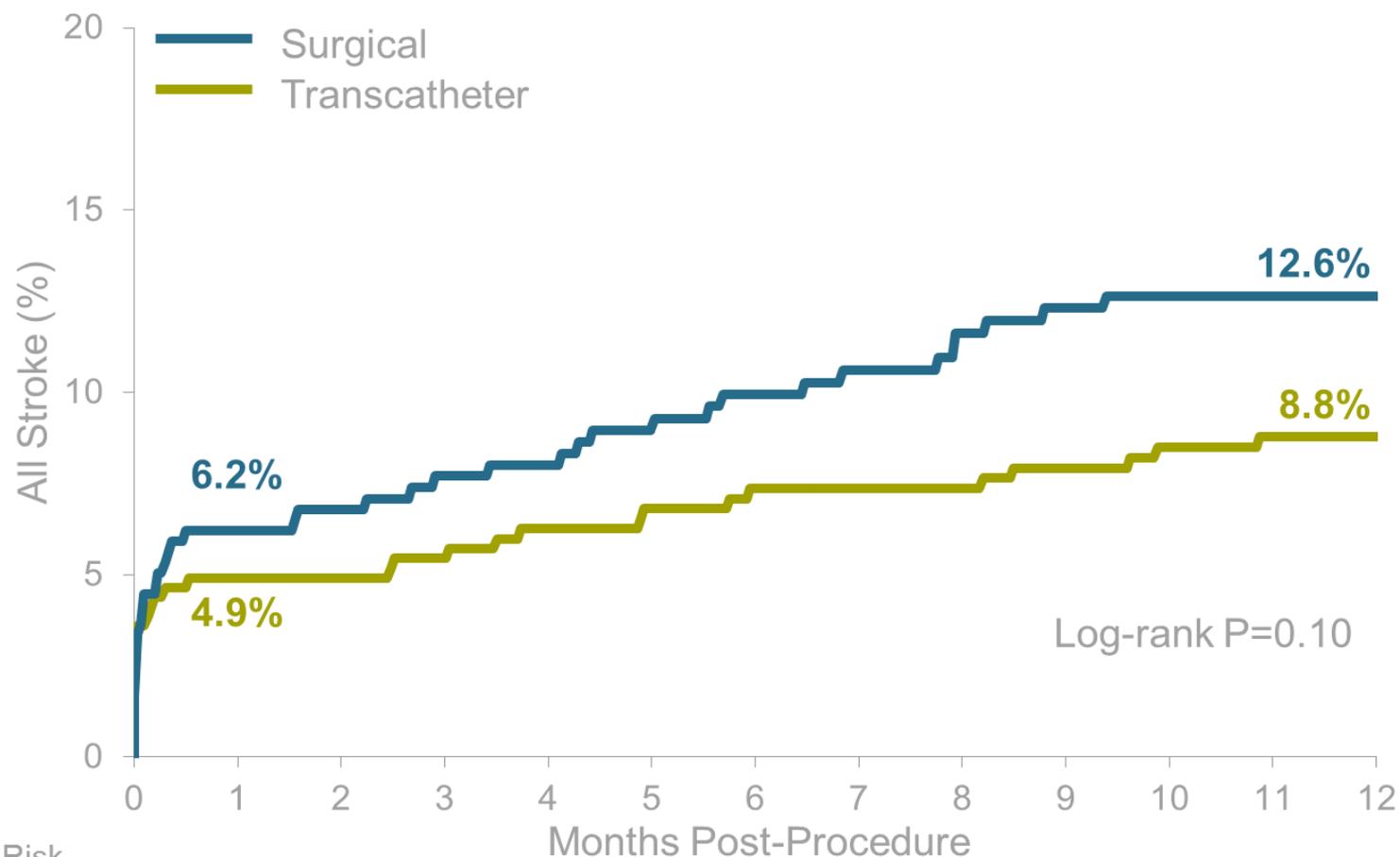


Leon et al, NEJM
Smith et al, NEJM
Kodali et al, ACC 2013
Leon et al, ACC 2013
Dewey et al, STS 2012

All Stroke : PARTNER A (ITT)



CoreValve Trial : All Stroke



No. at Risk

Surgical	357	322	274	249	
Transcatheter	390	363	334	314	27

What is the risk of stroke with surgery?

- **2.6% PARTNER -SAVR**
- **6.2% CoreValve - SAVR**

High Risk Surgical AVR and Stroke

Outcome	Patients (n=159)
Death (In-Hospital)	26 (16.4%)
Permanent Neurological Event	7 (4.4%)
Transient Neurological Event	4 (2.5%)

- Isolated AVR
- 2002-2007
- STS >10 at 4 academic institutions

Cardiovascular Surgery

Stroke After Aortic Valve Surgery Results From a Prospective Cohort

Steven R. Messé, MD; Michael A. Acker, MD; Scott E. Kasner, MD; Molly Fanning, BS;
Tania Giovannetti, PhD; Sarah J. Ratcliffe, PhD; Michel Bilello, MD, PhD;
Wilson Y. Szeto, MD; Joseph E. Bavaria, MD; W. Clark Hargrove, III, MD;
Emile R. Mohler III, MD; Thomas F. Floyd, MD;
for the Determining Neurologic Outcomes from Valve Operations (DeNOVO) Investigators

Conclusions—Clinical stroke after AVR was more common than reported previously, more than double for this same cohort in the Society for Thoracic Surgery database, and silent cerebral infarctions were detected in more than half of the patients undergoing AVR. Clinical stroke complicating AVR is associated with increased length of stay and mortality. (*Circulation*. 2014;129:2253-2261.)

AVR and Stroke

2008-2012 – 196 patients (U Penn)

Strokes = 34 patients (17%; 95% CI, 12-23%)

TIA = 4 patients (2%; 95% CI, 0 -4%)

NIHSS <5 = 22

NIHSS 5-9 = 4

NIHSS 10-15 = 3

NIHSS >15 = 5

POD 1 = 17 (58%)

POD 2-3 = 7 (21%)

POD 4-7 = 7 (21%)

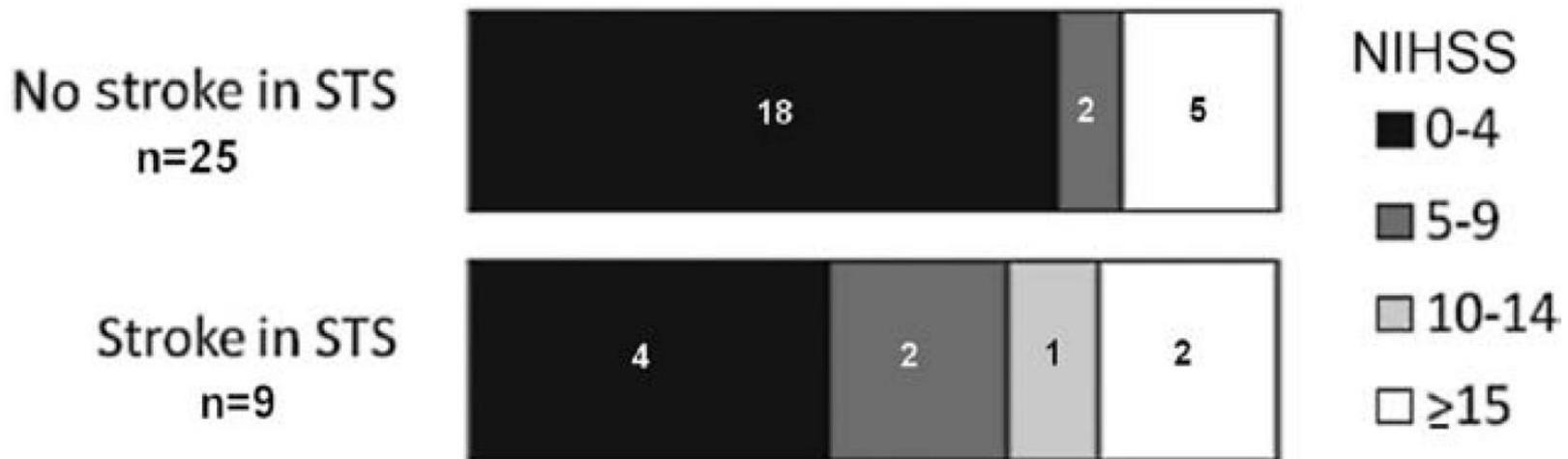
>POD 7 = 3 (9%)

AVR and Stroke

- A meta-analysis of 48 observational studies including 13,216 subjects ≥ 80 years old who underwent **isolated AVR** reported that stroke occurred in **2.4%**.
- A separate meta-analysis of 40 studies evaluating outcome from combined **aortic valve and coronary artery bypass grafting (CABG)** found a higher stroke rate of **3.7%**.
- The STS national database reported a stroke rate of **1.5%** from $>67,000$ **isolated AVR** procedures and **2.7%** from $>66,000$ subjects who underwent **AVR plus CABG**.
- The highest risks of neurologic complications have been reported in subjects undergoing **multivalve procedures**, with stroke occurring in **$\leq 9.7\%$** of subjects.

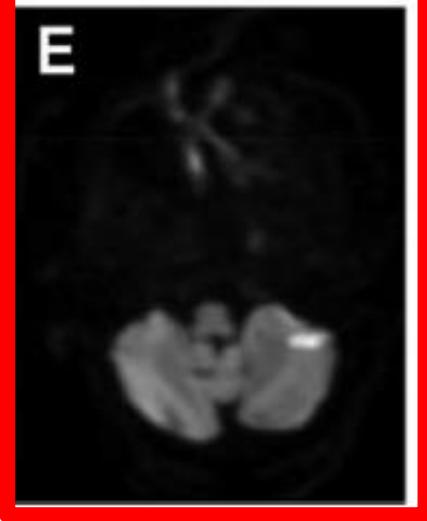
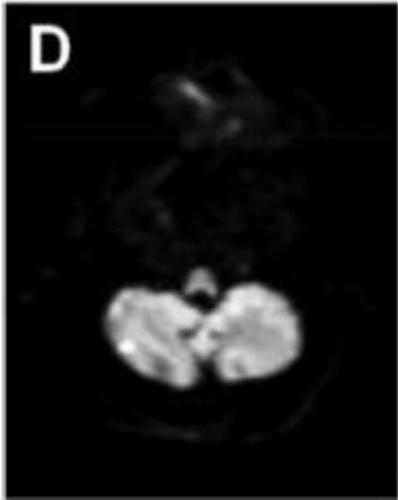
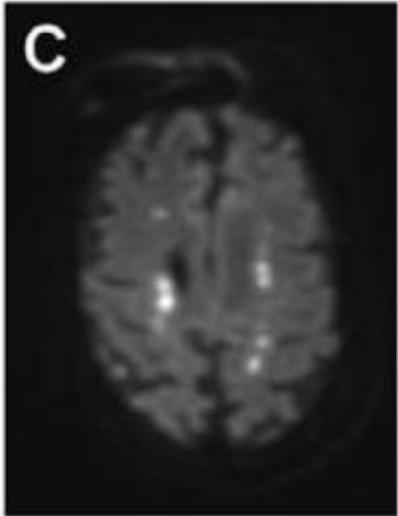
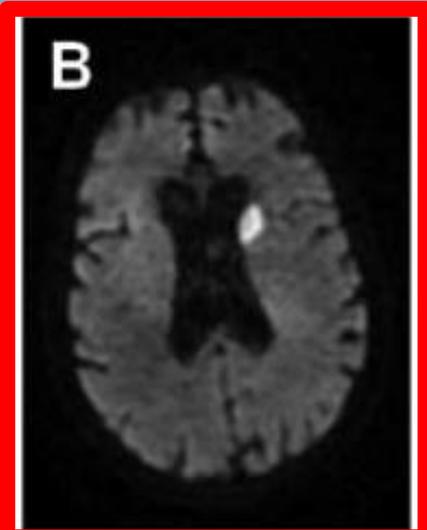
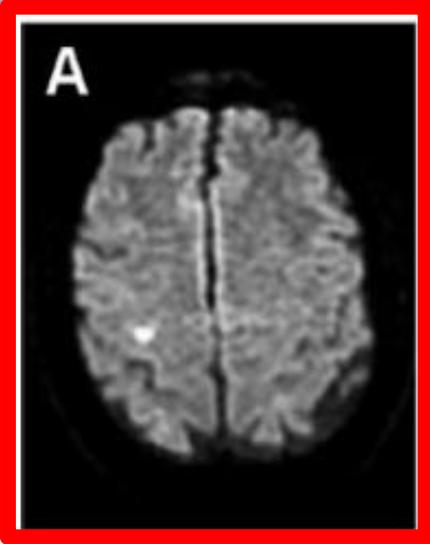
Stroke Detection and Reporting

25 “strokes” were not included in STS database



STS database reported 13 patients (6.6%) with stroke but 4 did not have stroke by DeNOVO (alcohol withdrawal, no deficit by day 7)

MRI (61% with lesions, 2.3/pt)



Stroke incidence and mortality after TAVI

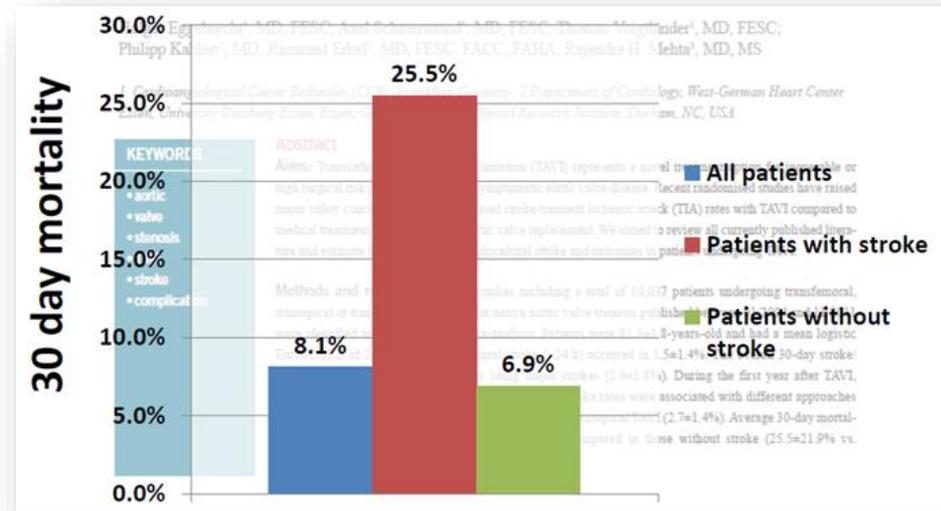
Meta-analysis of 10,037 published patients

Stroke remains a major TAVI complication...

Table 3. Incidence of stroke.

	Number of publications with available data (n)	Overall number of patients with available data (n)	Number of events (n)	Weighted mean±SD
Procedural stroke (<24h)	24	3041	47	1.5±1.4%
30-day stroke/TIA	53	10037	334	3.3±1.8%
30-day major stroke	42	5514	158	2.9±1.8%
30-day minor stroke/TIA	42	5514	53	1.0±1.3%
30-day overall mortality	52	10022	812	8.1±3.9%
30-day mortality in patients suffering stroke	29	4430	41	25.5±21.9%
30-day mortality in patients without stroke	29	4430	312	6.9±4.2%
6-month stroke	9	669	29	4.3±1.6%
12-month stroke	7	1507	78	5.2±3.4%

...which increases 30-day mortality >3 fold



Stroke remains a real risk

Clinical Outcome at 30 Days (I)



	Balloon-expandable (n=121)	Self-expandable (n=117)	p-value
Death			
From any cause	5/121 (4.1%)	6/117 (5.1%)	0.77
From CV causes	5/121 (4.1%)	5/117 (4.3%)	0.99
Stroke	7/121 (5.8%)	3/117 (2.6%)	0.33
Major	3/121 (2.5%)	3/117 (2.6%)	0.99
Minor	4/121 (3.3%)	0/117 (0.0%)	0.12
Myocardial infarction	1/121 (0.8%)	0/117 (0.0%)	0.99
Bleeding			
Life threatening	10/121 (8.3%)	14/117 (12.0%)	0.35
Major	23/121 (19.0%)	17/117 (14.5%)	0.36
Minor	11/121 (9.1%)	9/117 (7.7%)	0.70
Major or minor	34/121 (28.1%)	26/117 (22.2%)	0.30
Vascular complications			
All	17/121 (14.0%)	15/117 (12.8%)	0.78
Major	12/121 (9.9%)	13/117 (11.1%)	0.76
Minor	5/121 (4.1%)	2/117 (1.7%)	0.28

Risk factors for Neurologic Events

Multiphase, multivariable non-proportional hazard analysis

- *Early high peaking hazard phase*
- *Later constant hazard phase*

Risk Factor	Coefficient ± SD	P	R (%)
Early hazard phase			
TAVR	2.21±0.68	.001	59
Cerebrovascular disease	0.76±0.45	.09	44
(Smaller) indexed native aortic valve area in TAVR group	-11.8±5.1	.02	57
Constant hazard phase			
TAVR	0.40±0.43	0.4	22
(Higher) NYHA	0.95±0.40	.02	75
Stroke or TIA within 6-12 months	1.93±0.64	.002	60
Non-TF TAVR candidate	2.3±0.45	<.0001	96
History of PCI (less risk)	-1.60±0.63	.01	77
COPD (less risk)	-1.06±0.47	.03	79

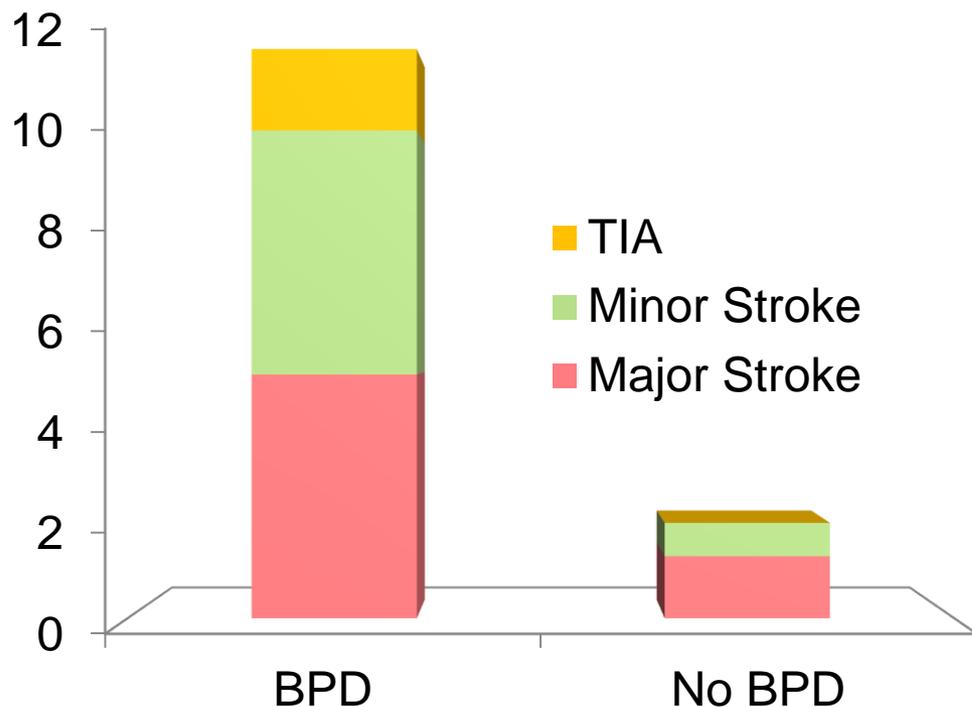
TAVR and Stroke : Registry Data

Registry	n	30 day	1 year	Prior stroke
FRANCE 2	3195	-	4.1	10
Canadian	339	2.3		22.7
PARTNER-EU	130	2.3	6.9	-
Australia NZ	118	1.7		-
UK-TAVI	870	4.1		-
Belgian	328	4.4		15
FRANCE	244	3.6		10.2
SOURCE	1038	2.6		-
European Registry	646	1.9		7.4
German	697	2.8		8.2
Italian	663	1.2	2.6	7.2

Predictors of Stroke, Neuro events or MRI findings

Author	N	Event rate	Approach	Clinical predictors	Anatomical predictors
Tay et al 2011	253	9%	TA/TF	H/O stroke/TIA	Carotid stenosis*
Nuis et al 2012	214	9%	TF	New onset AF	Baseline AR >3+
Amat Santos et al 2012	138	6.5%	TA/TF	New onset AF	None
Franco et al 2012	211	4.7%	TA/TF	None	Post-dilation
Miller et al 2012	344	9%	TA/TF	History of stroke Non TF-TAVR candidate	Smaller AVA
Cabau et al 2011	60	68% (MRI)	TA/TF	Male, History of CAD	Higher AVG
Fairbairn et al 2012	31	77% (MRI)	TF	Age	Aortic atheroma
Nombela-Franco et al 2012	1061	5.1%	TA/TF	Balloon postdilatation, valve dislodgement, New onset AF, PVD, Prior CVA	

Impact of Post-Dilatation



EDITORIAL COMMENT

Post-Dilating Transcatheter Heart Valves*

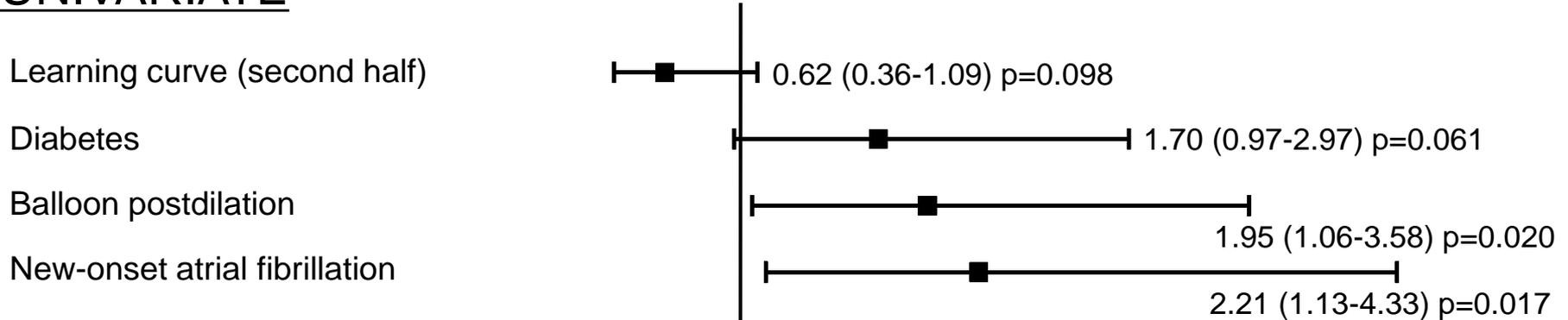
John G. Webb, MD, Ronald K. Binder, MD

Vancouver, British Columbia, Canada

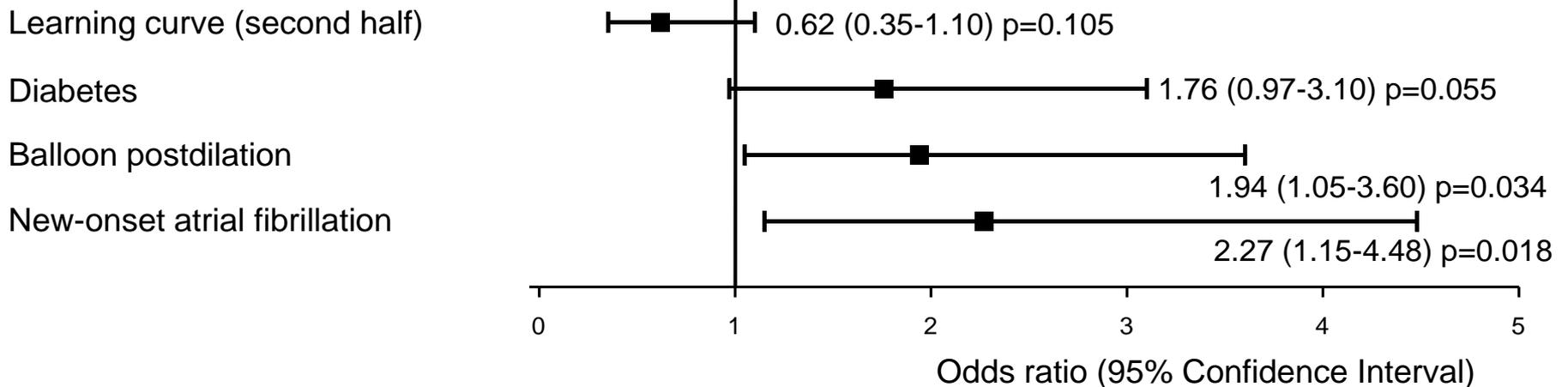
To what degree was post-dilatation just a marker of a more calcified valve intrinsically more likely to release embolic material at the time of valve positioning or expansion? We do not know.

Predictors of Early (30-Day) CVEs

UNIVARIATE



MULTIVARIATE



Predictors of Late CVEs (>30-day)

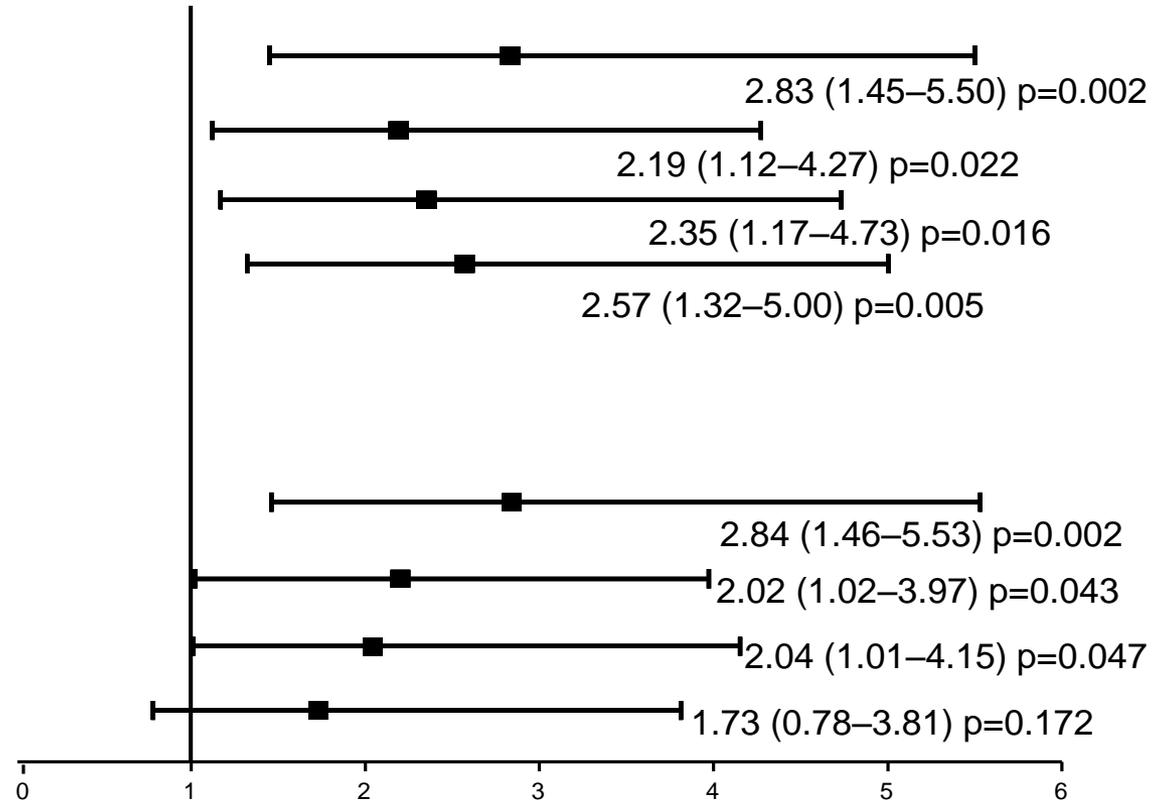
UNIVARIATE

Chronic atrial fibrillation

Peripheral vascular disease

Cerebrovascular disease

Anticoagulation treatment at hospital discharge



MULTIVARIATE

Chronic atrial fibrillation

Peripheral vascular disease

Cerebrovascular disease

Anticoagulation treatment at hospital discharge

Hazard ratio (95% Confidence Interval)

Conclusions

- **Stroke risk is somewhat less in patients as we move to lower risk population**
- **Stroke risk is not negligible**
- **Variability of stroke ascertainment may be the main reason for differences in stroke reporting**
- **Efforts to reduce stroke risk should continue to make TAVR and other transcatheter procedures.**