Strokes After TAVR

Incidence (past and present)
Multi-factorial Origin

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All faculty disclosures are available on the CRF Events App and online at www.crf.org/tct

Stroke

- How common is stroke after TAVR
  - Is it increasing?
  - Is it more with TF vs TA?
  - Is it different in SE or BE valves?
  - How does this compare to surgery?
- Timing of stroke
  - Procedural versus non procedural
- Predictors of stroke after TAVR
- Prevention Methods

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIALS

Transcatheter Aortic-Valve Implantation — At What Price?

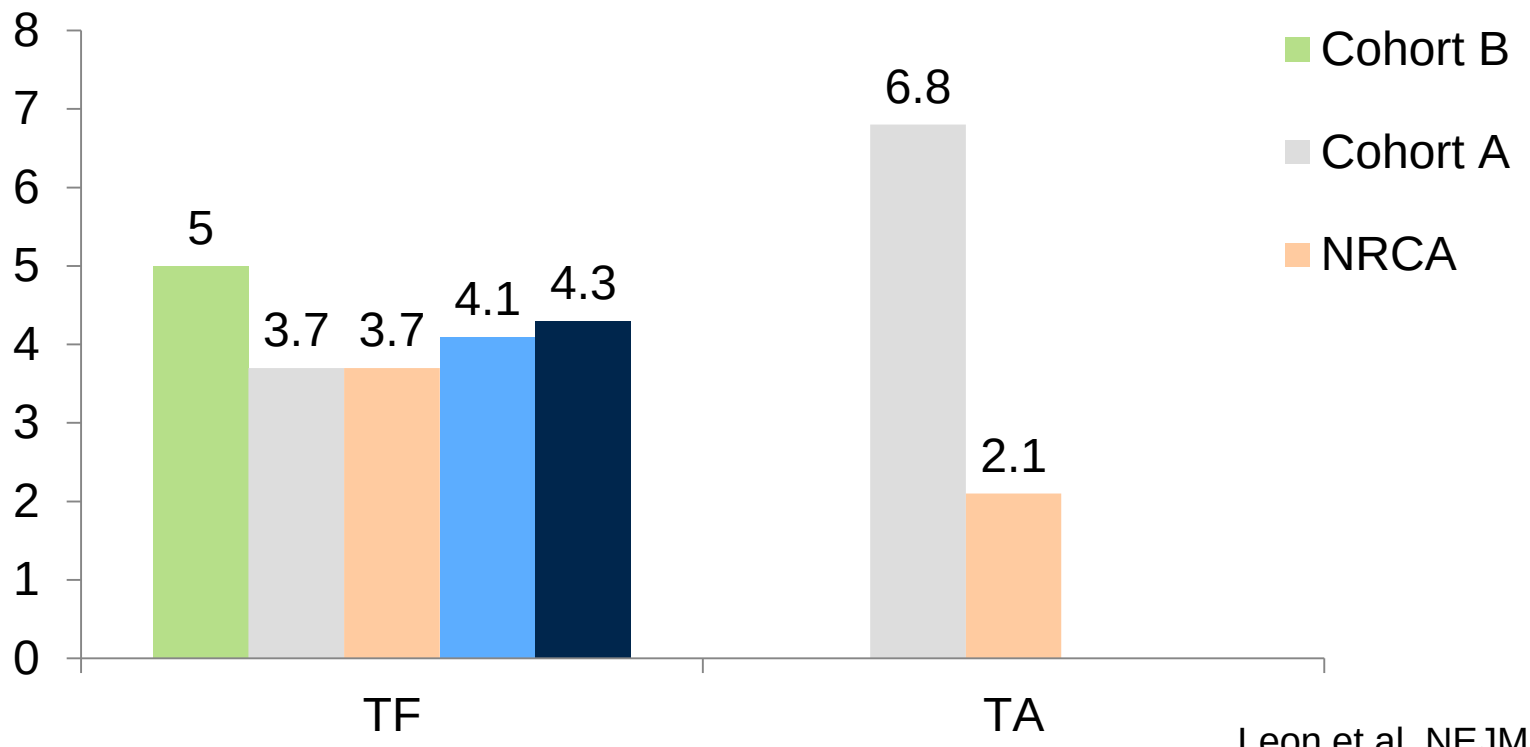
Hartzell V. Schaff, M.D.

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.[1] 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

30 Days - All Stroke from PARTNER Trials



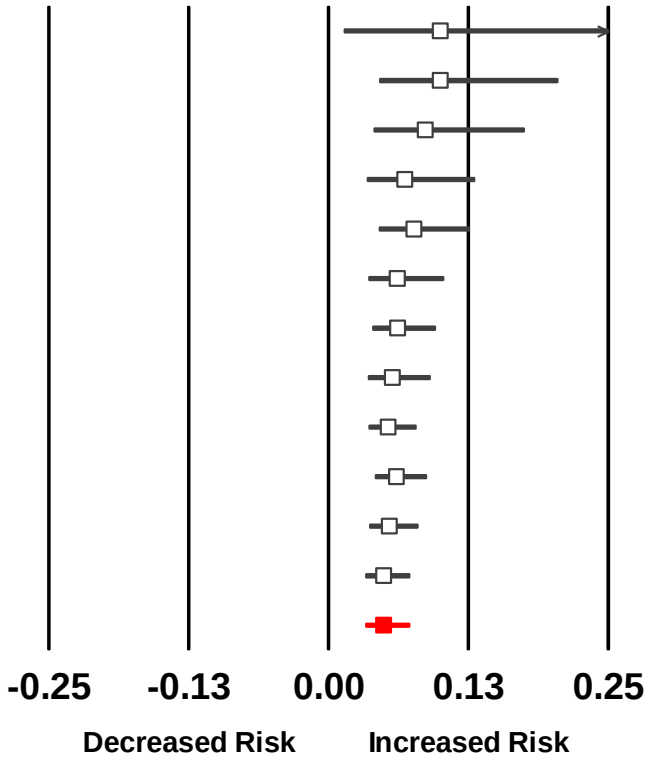
Leon et al, NEJM
Smith et al, NEJM
Kodali et al, ACC 2013
Leon et al, ACC 2013
Dewey et al, STS 2012

Stroke : Feasibility Trials

Study name	Cumulative statistics					
	Point	Lower limit	Upper limit	Z-Value	p-Value	Total
24 F	0.100	0.014	0.467	-2.084	0.037	1 / 10
21 F	0.100	0.046	0.205	-5.106	0.000	6 / 60
Walther***	0.087	0.041	0.175	-5.721	0.000	6 / 90
Walther **	0.068	0.034	0.131	-7.108	0.000	8 / 149
REVIVAL	0.076	0.045	0.126	-8.765	0.000	13 / 204
REVIVE 2	0.061	0.036	0.103	-9.466	0.000	16 / 310
REVIVAL 2	0.062	0.039	0.096	-11.244	0.000	18 / 350
Walther*	0.057	0.035	0.091	-10.909	0.000	18 / 400
Vancouver Exp	0.053	0.036	0.078	-13.662	0.000	25 / 568
18 F	0.061	0.042	0.088	-13.517	0.000	37 / 694
PARTNER EU	0.054	0.037	0.080	-13.533	0.000	40 / 824
Traverce	0.049	0.033	0.073	-13.969	0.000	44 / 992
	0.049	0.033	0.073	-13.969	0.000	

4.9%

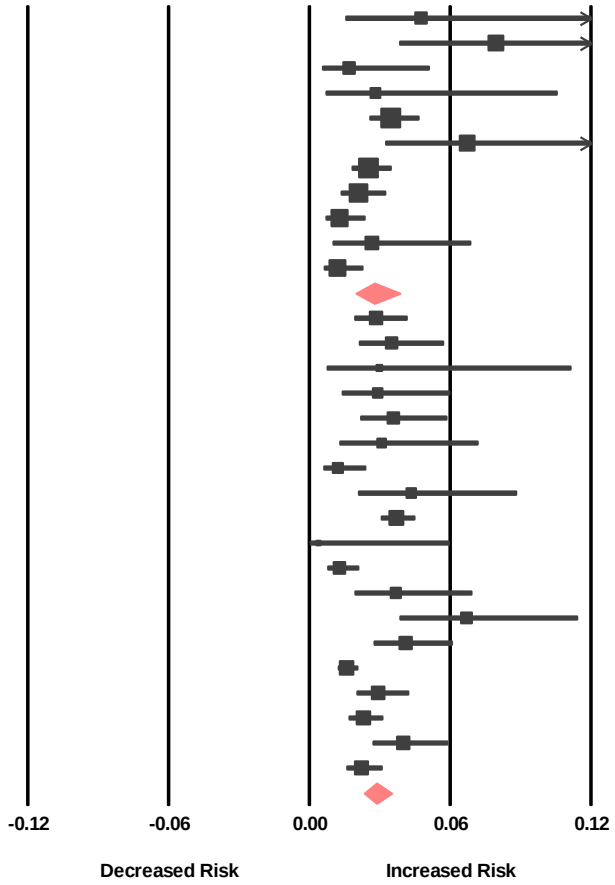
Cumulative event rate (95% CI)



Athappan et al, JACC 2014

In hospital or 30 day stroke TA versus TF (Major Registries)

Group by Subgroup within study	Study name	Subgroup within study		Event rate	Lower limit	Upper limit	Z-Value	p-Value	Total
TA	ANZ Source	TA		0.048	0.015	0.138	-5.064	0.000	3 / 63
TA	Belgium	TA		0.080	0.038	0.158	-6.215	0.000	7 / 88
TA	Canada	TA		0.017	0.005	0.051	-6.973	0.000	3 / 177
TA	France	TA		0.028	0.007	0.106	-4.937	0.000	2 / 71
TA	GARY	TA		0.035	0.026	0.047	-20.919	0.000	41 / 1181
TA	PARTNER I cohort A	TA		0.067	0.032	0.135	-6.717	0.000	7 / 104
TA	SOURCE Registry	TA		0.025	0.018	0.035	-21.343	0.000	35 / 1387
TA	SOURCE XT	TA		0.021	0.013	0.033	-16.576	0.000	19 / 906
TA	I-TA Registry	TA		0.013	0.007	0.024	-13.623	0.000	10 / 774
TA	PREVAIL TA	TA		0.027	0.010	0.069	-7.098	0.000	4 / 150
TA	EORP/TCVT	TA		0.012	0.006	0.023	-13.149	0.000	9 / 749
TA			2.8%	0.028	0.020	0.039	-20.357	0.000	
TF	ADVANCE	TF		0.028	0.019	0.042	-17.402	0.000	25 / 879
TF	ANZ CoreValve	TF		0.035	0.021	0.057	-12.613	0.000	15 / 428
TF	ANZ Source	TF		0.030	0.007	0.112	-4.849	0.000	2 / 67
TF	Belgium	TF		0.029	0.014	0.060	-9.137	0.000	7 / 240
TF	Brazil	TF		0.036	0.022	0.059	-12.515	0.000	15 / 418
TF	Canada	TF		0.031	0.013	0.072	-7.587	0.000	5 / 162
TF	Italian CoreValve Registry	TF		0.012	0.006	0.024	-12.367	0.000	8 / 659
TF	France	TF		0.043	0.021	0.088	-7.998	0.000	7 / 161
TF	GARY	TF		0.037	0.031	0.045	-31.948	0.000	100 / 2694
TF	Greece	TF		0.004	0.000	0.060	-3.905	0.000	0 / 126
TF	Ibero-American Registry	TF		0.013	0.008	0.021	-16.715	0.000	15 / 1170
TF	PARTNER I cohort A	TF		0.037	0.019	0.069	-9.605	0.000	9 / 244
TF	PARTNER I cohort B	TF		0.067	0.038	0.114	-8.810	0.000	12 / 179
TF	PARTNER II	TF		0.041	0.027	0.061	-14.796	0.000	23 / 560
TF	EORP/TCVT	TF		0.016	0.012	0.021	-30.059	0.000	54 / 3390
TF	SOURCE Registry	TF		0.029	0.020	0.042	-17.911	0.000	27 / 920
TF	SOURCE XT	TF		0.023	0.017	0.031	-23.135	0.000	39 / 1694
TF	U.K TAVI	TF		0.040	0.027	0.059	-15.246	0.000	24 / 599
TF	18F EE Registry	TF		0.022	0.016	0.031	-21.487	0.000	33 / 1483
TF			2.9%	0.029	0.023	0.035	-33.155	0.000	



Athappan et al, JACC 2014

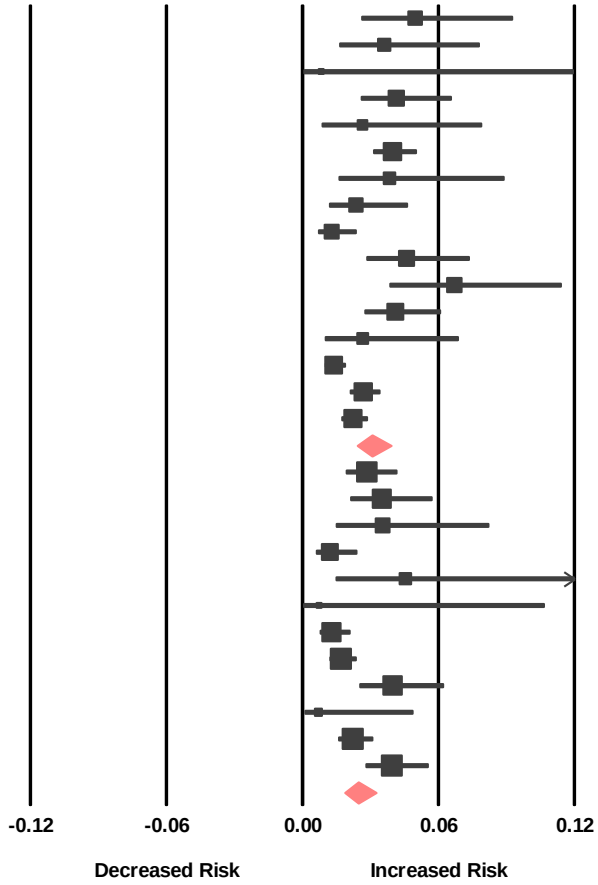
In Hospital or 30 Day Stroke ES versus MC – Major Registires

Group by Subgroup within study	Study name	Subgroup within study	Event rate	Lower limit	Upper limit	Z-Value	Total
ES	Belgium	ES	0.050	0.026	0.093	-8.628	9 / 181
ES	France	ES	0.036	0.016	0.078	-7.896	6 / 166
ES	Greece	ES	0.008	0.001	0.120	-3.365	0 / 59
ES	U.K TAVI	ES	0.041	0.026	0.066	-12.678	17 / 410
ES	Asia TAVI	ES	0.027	0.009	0.079	-6.155	3 / 113
ES	FRANCE 2	ES	0.040	0.031	0.050	-25.15365	/ 1634
ES	ANZ Source	ES	0.038	0.016	0.089	-7.058	5 / 130
ES	Canada	ES	0.024	0.012	0.046	-10.404	8 / 339
ES	I-TA Registry	ES	0.013	0.007	0.024	-13.623	10 / 774
ES	PARTNER I cohort A	ES	0.046	0.028	0.074	-11.848	16 / 348
ES	PARTNER I cohort B	ES	0.067	0.038	0.114	-8.810	12 / 179
ES	PARTNER II	ES	0.041	0.027	0.061	-14.796	23 / 560
ES	PREVAIL TA	ES	0.027	0.010	0.069	-7.098	4 / 150
ES	EORP/TCVT	ES	0.014	0.010	0.019	-25.42736	/ 2604
ES	SOURCE Registry	ES	0.027	0.021	0.034	-27.88062	/ 2307
ES	SOURCE XT	ES	0.022	0.017	0.029	-28.46758	/ 2600
ES			0.031	0.024	0.039	-27.136	
MC	ADVANCE	MC	0.028	0.019	0.042	-17.402	25 / 879
MC	ANZ CoreValve	MC	0.035	0.021	0.057	-12.613	15 / 428
MC	Belgium	MC	0.035	0.015	0.082	-7.254	5 / 141
MC	Italian CoreValve Registry	MC	0.012	0.006	0.024	-12.367	8 / 659
MC	France	MC	0.045	0.015	0.132	-5.152	3 / 66
MC	Greece	MC	0.007	0.000	0.107	-3.456	0 / 67
MC	Ibero-American Registry	MC	0.013	0.008	0.021	-16.71515	/ 1170
MC	EORP/TCVT	MC	0.017	0.012	0.024	-23.11533	/ 1943
MC	U.K TAVI	MC	0.040	0.025	0.062	-13.231	18 / 452
MC	Asia TAVI	MC	0.007	0.001	0.049	-4.917	1 / 140
MC	18F EE Registry	MC	0.022	0.016	0.031	-21.48733	/ 1483
MC	FRANCE 2	MC	0.039	0.028	0.056	-17.415	31 / 785
MC			0.025	0.019	0.032	-25.270	

3.1%

2.5%

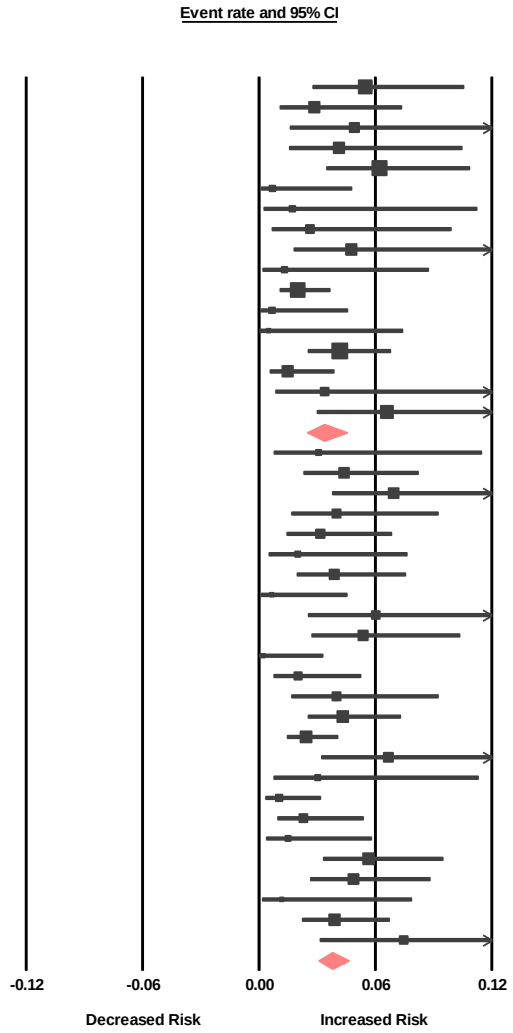
Event rate and 95% CI



Athappan et al, JACC 2014

Single Center (TF versus TA)

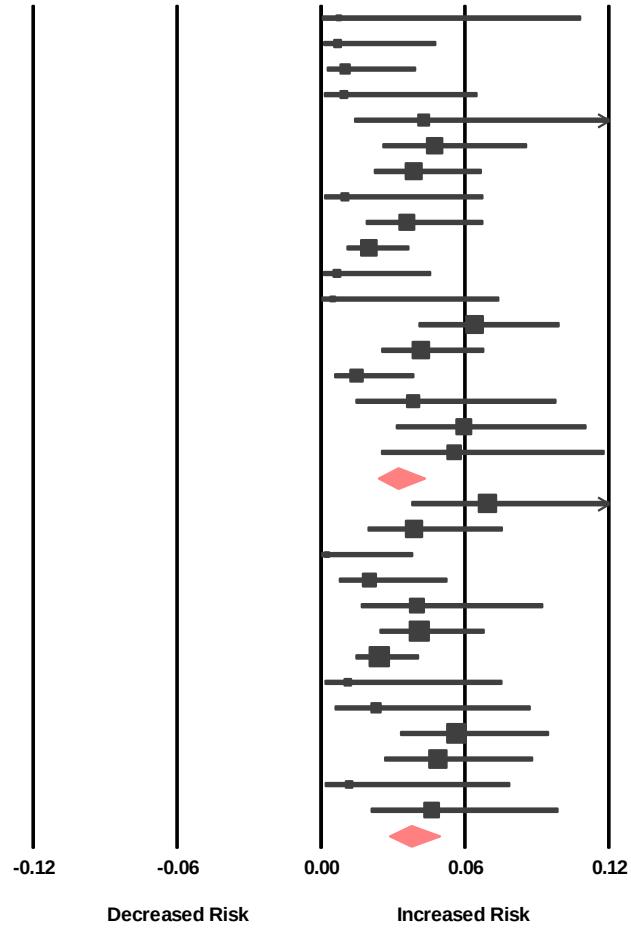
Group by Subgroup within study	Study name	Subgroup within study	Event rate	Lower limit	Upper limit	Z-Value	p-Value	Total
TA	Quebec City	TA	0.055	0.028	0.106	-7.831	0.000	8 / 146
TA	Vancouver	TA	0.029	0.011	0.074	-6.951	0.000	4 / 140
TA	Rouen	TA	0.049	0.016	0.142	-5.002	0.000	3 / 61
TA	Gottingen	TA	0.041	0.016	0.105	-6.161	0.000	4 / 97
TA	Hamburg UHC	TA	0.062	0.035	0.109	-8.717	0.000	11 / 177
TA	Munich	TA	0.007	0.001	0.048	-4.938	0.000	1 / 143
TA	Padova	TA	0.017	0.002	0.112	-4.008	0.000	1 / 58
TA	Bern	TA	0.026	0.007	0.099	-5.039	0.000	2 / 76
TA	London, kings	TA	0.048	0.018	0.120	-5.847	0.000	4 / 84
TA	Skejby	TA	0.013	0.002	0.088	-4.289	0.000	1 / 76
TA	Berlin -German Heart	TA	0.020	0.011	0.037	-12.183	0.000	10 / 500
TA	Cologne	TA	0.007	0.001	0.046	-4.987	0.000	1 / 150
TA	Frankfurt	TA	0.005	0.000	0.074	-3.741	0.000	0 / 100
TA	Leipzig	TA	0.042	0.025	0.068	-11.888	0.000	15 / 360
TA	Stuttgart	TA	0.015	0.006	0.039	-8.332	0.000	4 / 270
TA	Leiden	TA	0.034	0.008	0.126	-4.656	0.000	2 / 59
TA	London, guys	TA	0.066	0.030	0.139	-6.276	0.000	6 / 91
TA		3.4%	0.034	0.025	0.045	-21.255	0.000	
TF	Quebec City	TF	0.031	0.008	0.115	-4.803	0.000	2 / 65
TF	Vancouver	TF	0.044	0.023	0.082	-9.038	0.000	9 / 205
TF	Créteil	TF	0.069	0.038	0.124	-7.917	0.000	10 / 144
TF	Paris	TF	0.040	0.017	0.093	-6.963	0.000	5 / 125
TF	Rouen	TF	0.032	0.014	0.068	-8.252	0.000	6 / 190
TF	Berlin -Charite	TF	0.020	0.005	0.076	-5.449	0.000	2 / 100
TF	Bonn	TF	0.039	0.020	0.076	-8.898	0.000	8 / 206
TF	Essen	TF	0.007	0.001	0.045	-4.994	0.000	1 / 151
TF	Gottingen	TF	0.060	0.025	0.137	-5.955	0.000	5 / 83
TF	Hamburg UHC	TF	0.054	0.027	0.104	-7.895	0.000	8 / 149
TF	Heidelberg	TF	0.002	0.000	0.033	-4.345	0.000	0 / 234
TF	Bochum	TF	0.020	0.008	0.053	-7.684	0.000	4 / 198
TF	Lubeck	TF	0.040	0.017	0.093	-6.963	0.000	5 / 125
TF	Munich	TF	0.043	0.025	0.073	-10.926	0.000	13 / 301
TF	Siegburg	TF	0.024	0.014	0.041	-13.647	0.000	14 / 576
TF	Jerusalem	TF	0.067	0.032	0.133	-6.746	0.000	7 / 105
TF	Bologna	TF	0.030	0.008	0.113	-4.826	0.000	2 / 66
TF	Milan	TF	0.010	0.003	0.032	-7.840	0.000	3 / 287
TF	Catania	TF	0.023	0.010	0.054	-8.293	0.000	5 / 218
TF	Padova	TF	0.015	0.004	0.058	-5.870	0.000	2 / 133
TF	Rotterdam	TF	0.057	0.033	0.095	-9.858	0.000	13 / 230
TF	Malaga	TF	0.049	0.026	0.088	-9.161	0.000	10 / 205
TF	Santiago de Compostela	TF	0.012	0.002	0.079	-4.405	0.000	1 / 85
TF	Bern	TF	0.039	0.022	0.067	-10.886	0.000	12 / 308
TF	London, kings	TF	0.075	0.031	0.167	-5.416	0.000	5 / 67
TF		3.8%	0.038	0.031	0.046	-30.053	0.000	



Athappan et al, JACC 2014

30 day or in hospital stroke MC versus ES – single center

Group by Subgroup within study	Study name	Subgroup within study		Event rate	Lower limit	Upper limit	Z-Value	p-Value	Total
ES	Heidelberg	ES		0.007	0.000	0.108	-3.445	0.001	0 / 66
ES	Munich	ES		0.007	0.001	0.048	-4.938	0.000	1 / 143
ES	Milan	ES		0.010	0.003	0.039	-6.451	0.000	2 / 198
ES	Padova	ES		0.010	0.001	0.065	-4.612	0.000	1 / 104
ES	Bern	ES		0.043	0.014	0.125	-5.263	0.000	3 / 70
ES	Quebec City	ES		0.047	0.026	0.086	-9.262	0.000	10 / 211
ES	Vancouver	ES		0.039	0.022	0.067	-10.910	0.000	12 / 310
ES	Skejby	ES		0.010	0.001	0.068	-4.572	0.000	1 / 100
ES	Rouen	ES		0.036	0.019	0.067	-9.696	0.000	9 / 251
ES	Berlin -German Heart	ES		0.020	0.011	0.037	-12.183	0.000	10 / 500
ES	Cologne	ES		0.007	0.001	0.046	-4.987	0.000	1 / 150
ES	Frankfurt	ES		0.005	0.000	0.074	-3.741	0.000	0 / 100
ES	Hamburg UHC	ES		0.064	0.041	0.099	-11.007	0.000	18 / 281
ES	Leipzig	ES		0.042	0.025	0.068	-11.888	0.000	15 / 360
ES	Stuttgart	ES		0.015	0.006	0.039	-8.332	0.000	4 / 270
ES	Leiden	ES		0.038	0.015	0.098	-6.313	0.000	4 / 104
ES	London - Kings	ES		0.060	0.031	0.111	-8.025	0.000	9 / 151
ES	London -Guys	ES		0.056	0.025	0.118	-6.744	0.000	6 / 108
ES			3.2%	0.032	0.024	0.043	-21.790	0.000	
MC	Créteil	MC		0.069	0.038	0.124	-7.917	0.000	10 / 144
MC	Bonn	MC		0.039	0.020	0.076	-8.898	0.000	8 / 206
MC	Heidelberg	MC		0.002	0.000	0.038	-4.237	0.000	0 / 201
MC	Bochum	MC		0.020	0.008	0.053	-7.684	0.000	4 / 198
MC	Lubeck	MC		0.040	0.017	0.093	-6.963	0.000	5 / 125
MC	Munich	MC		0.041	0.024	0.068	-11.545	0.000	14 / 341
MC	Siegburg	MC		0.024	0.014	0.041	-13.647	0.000	14 / 576
MC	Milan	MC		0.011	0.002	0.075	-4.452	0.000	1 / 89
MC	Padova	MC		0.023	0.006	0.087	-5.241	0.000	2 / 87
MC	Rotterdam	MC		0.057	0.033	0.095	-9.858	0.000	13 / 230
MC	Malaga	MC		0.049	0.026	0.088	-9.161	0.000	10 / 205
MC	Santiago de Compostela	MC		0.012	0.002	0.079	-4.405	0.000	1 / 85
MC	Bern	MC		0.046	0.021	0.099	-7.245	0.000	6 / 130
MC			3.8%	0.038	0.028	0.049	-22.231	0.000	

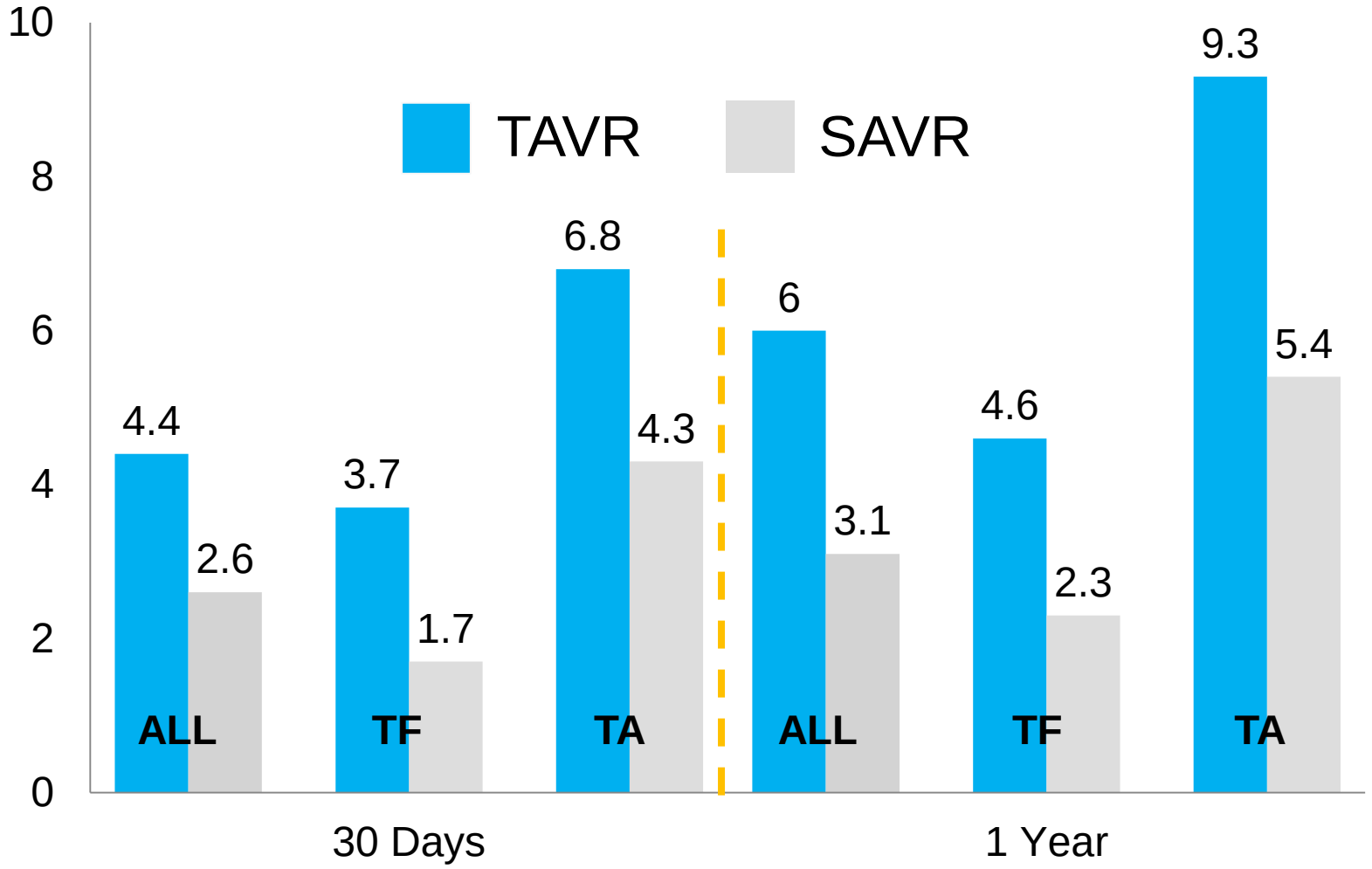


Athappan et al, JACC 2014

Stroke

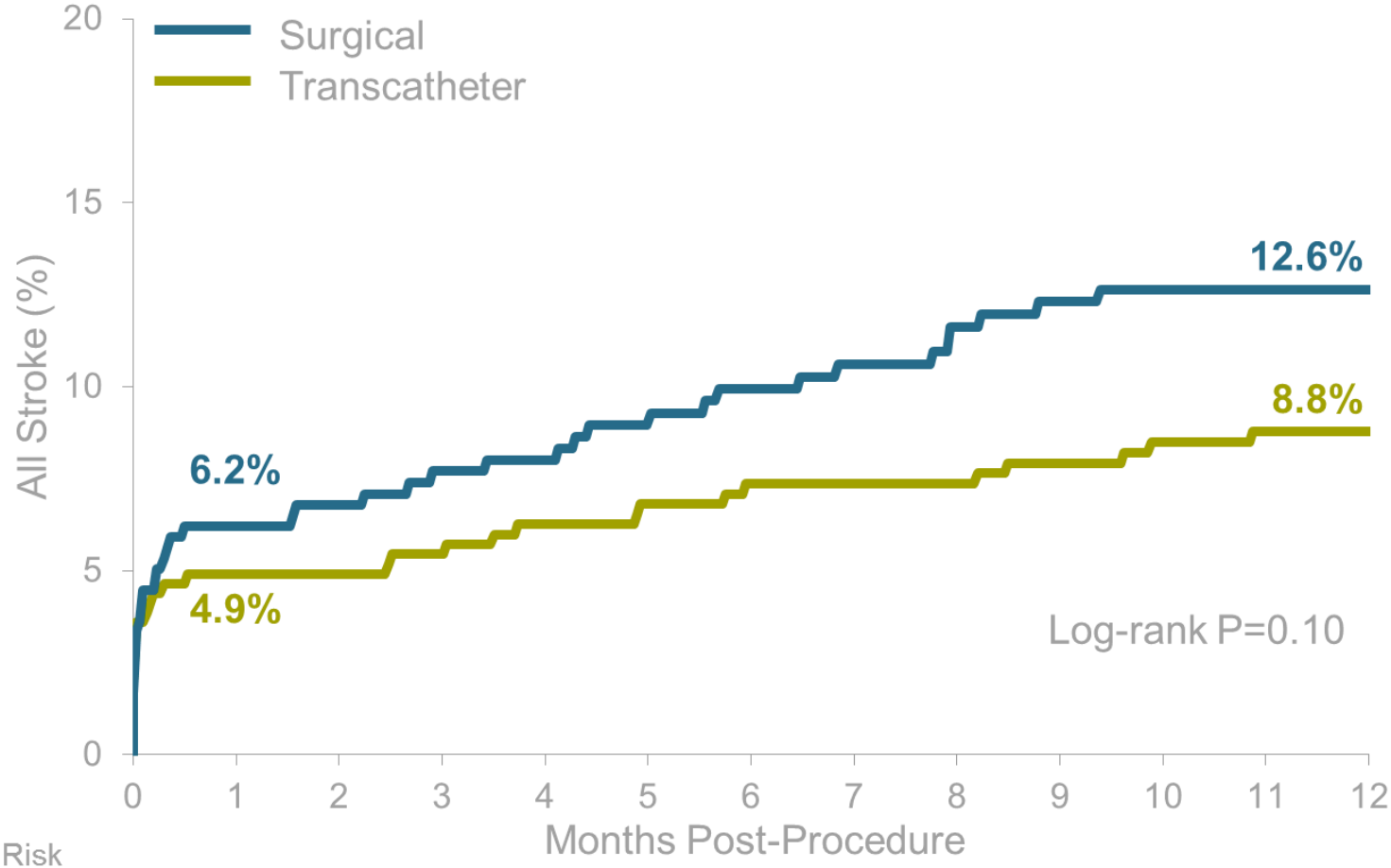
- How common is stroke after TAVR
  - Is it increasing?
  - Is it more with TF vs TA?
  - Is it different in SE or BE valves?
  - How does this compare to surgery?
- Timing of stroke
  - Procedural versus non procedural
- Predictors of stroke after TAVR
- Prevention Methods

All Stroke : PARTNER A (ITT)



Smith et al, NEJM, June 2011

CoreValve Trial : All Stroke



No. at Risk					
Surgical	357	322	274	249	
Transcatheter	390	363	334	314	

Adams, NEJM, 2014

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

Thourani et al, Ann Thorac Surg 2011;91:49 –56

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%)

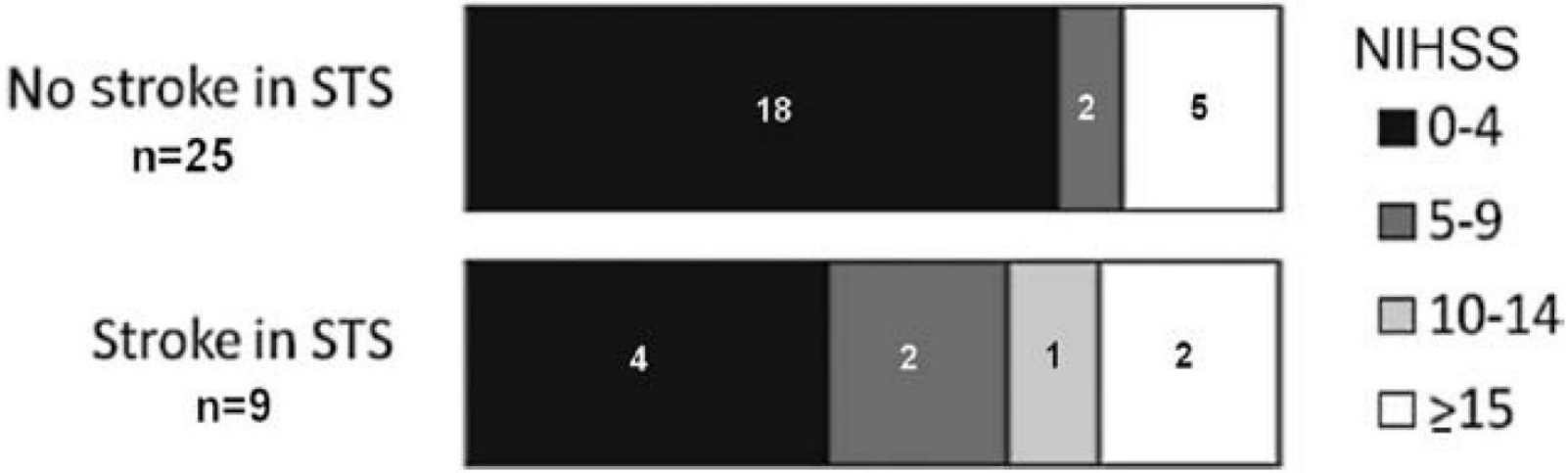
Masse, circulation, 2014

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 ≤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)

Masse, circulation, 2014

Stroke

- How common is stroke after TAVR
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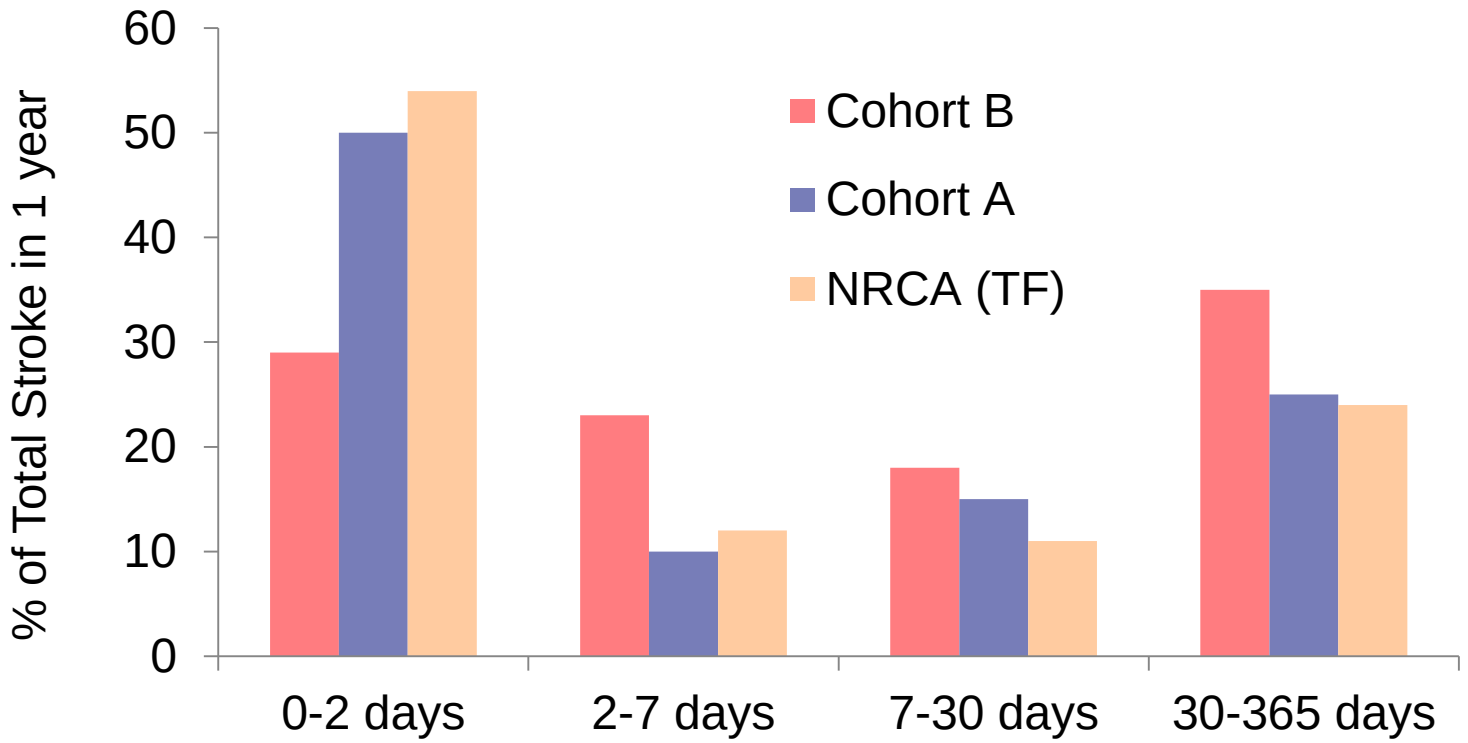
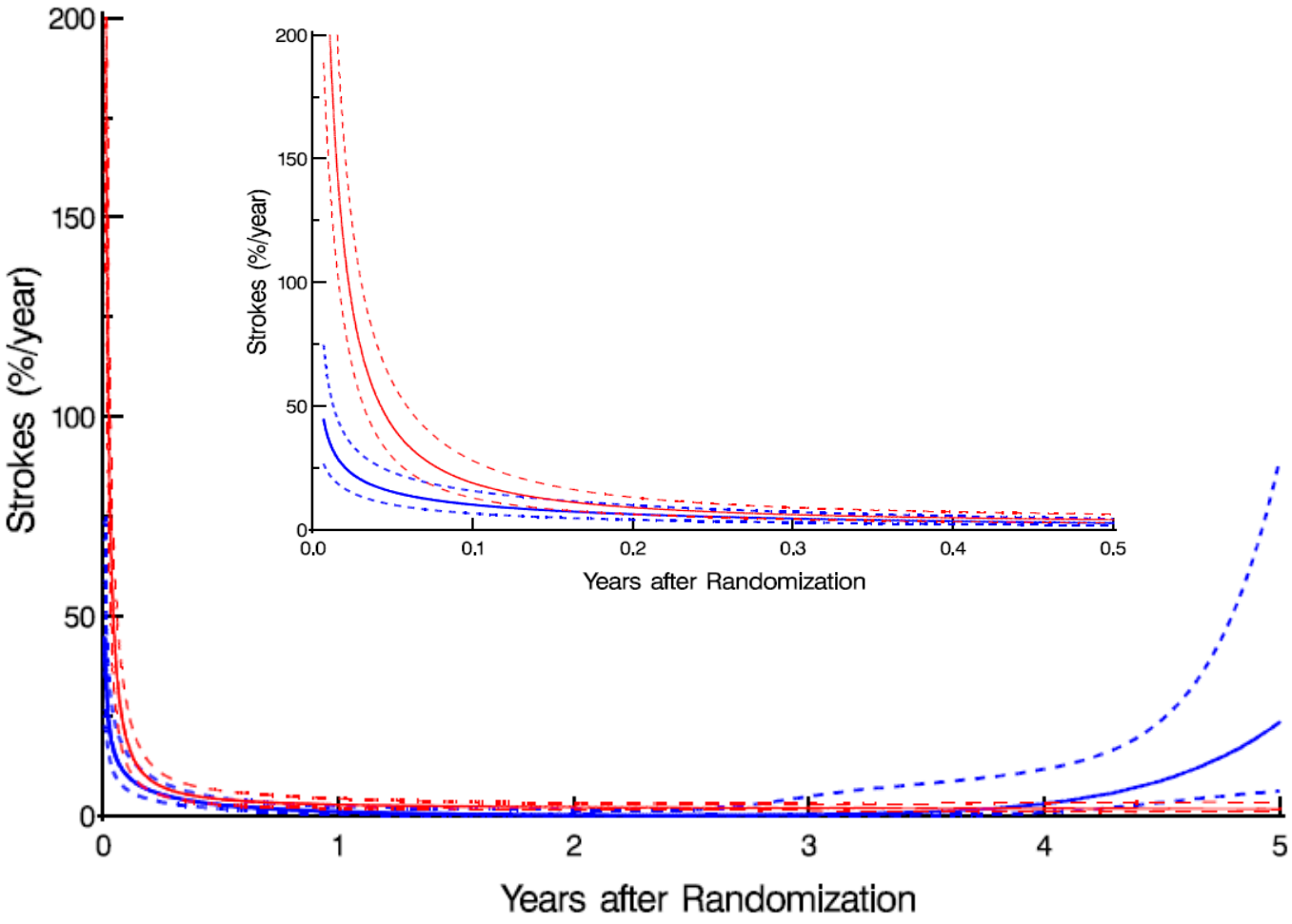
Stroke Timing within 1 year

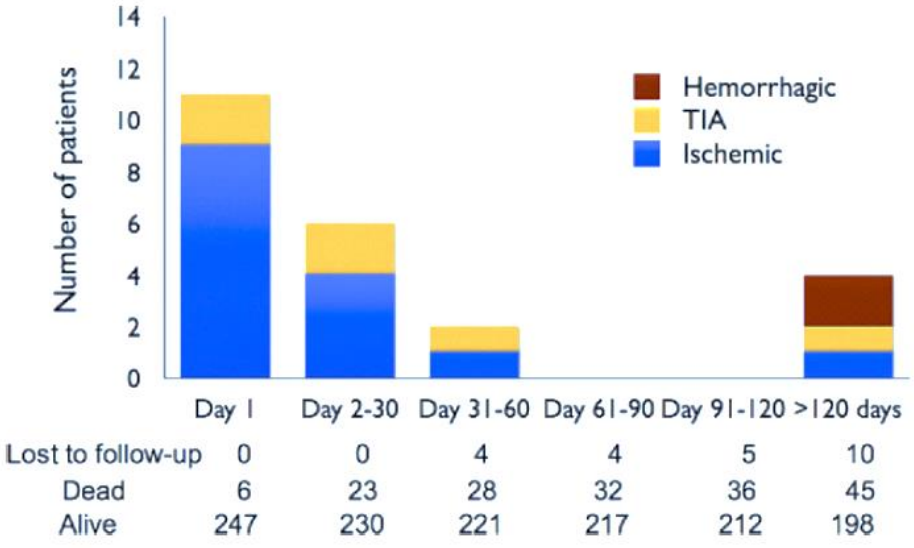


Leon et al, NEJM
Smith et al, NEJM
Kodali et al, ACC 2013

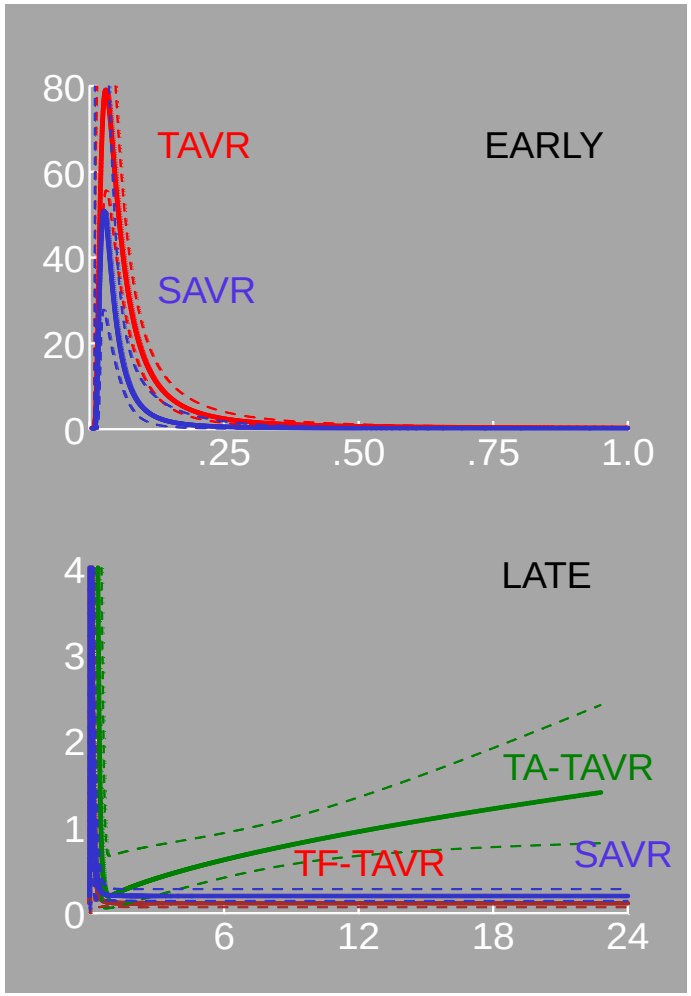
Stroke Analysis : Timing PARTNER 1B Instantaneous Risk of Stroke



Timing of Neurological Event
Emboli Prevention versus Pharmacotherapy



Tay et al, J Am Coll Cardiol Intv 2011;4:1290 –7



Miller et al, 2012;143:832-43

Stroke

- How common is stroke after TAVR
  - Is it increasing?
  - Is it more with TF vs TA?
  - Is it different in SE or BE valves?
  - How does this compare to surgery?
- Timing of stroke
  - Procedural versus non procedural
- Predictors of stroke after TAVR
- Prevention Methods

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

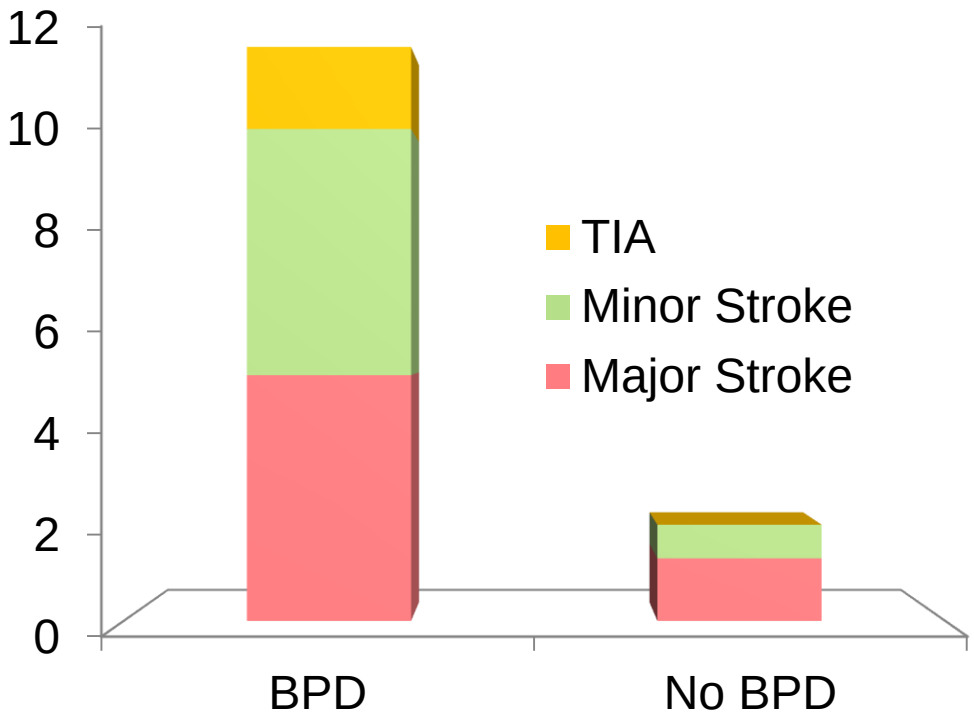
TAVR and Stroke : Registry Data

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-dilation 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.

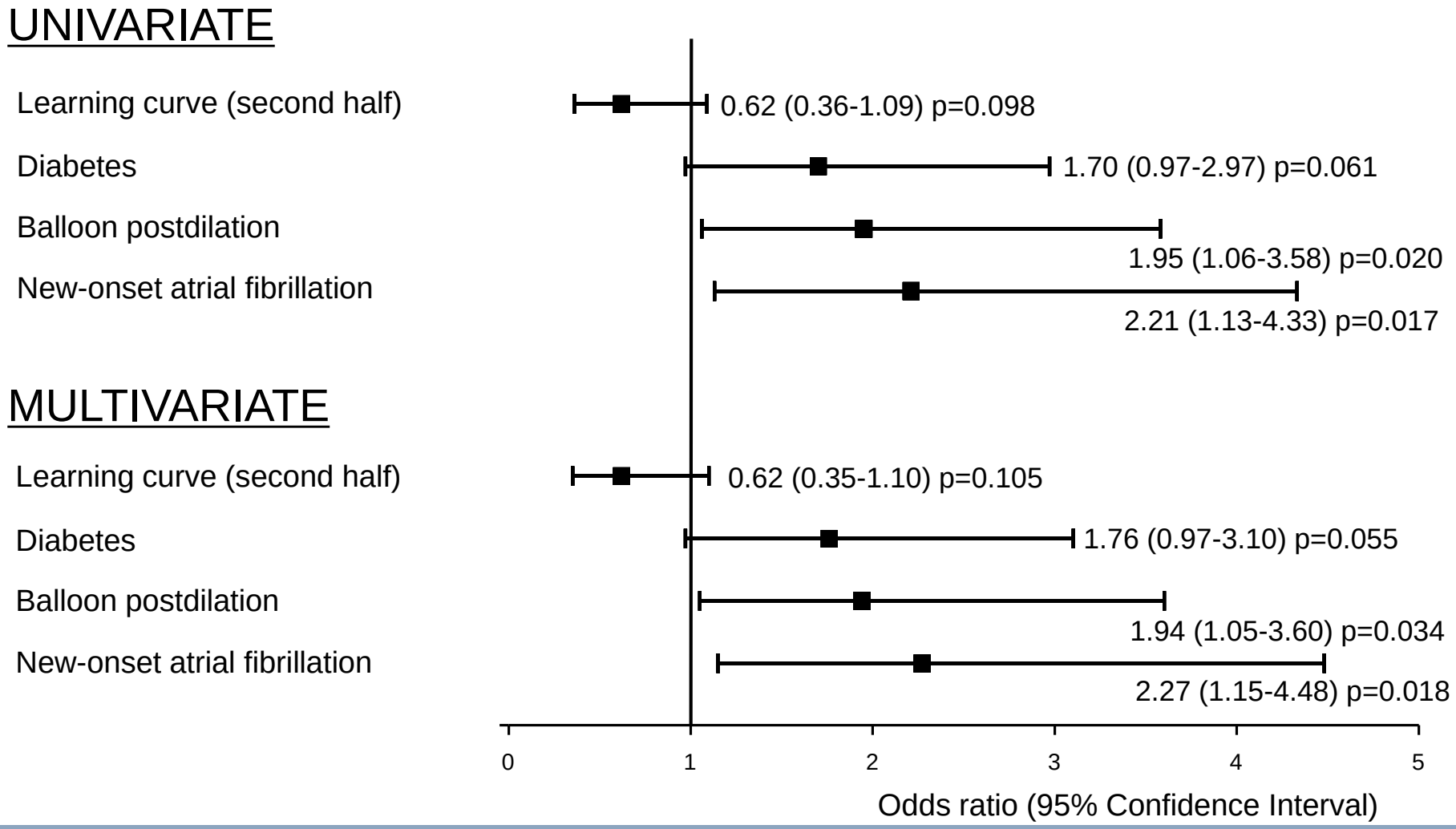
Nombela-Franco et al, J Am Coll Cardiol Intv 2012;5:499 –512

Canadian Experience

- **1061 Patients**
- **5 centers**
  - **679 (65%) Balloon expandable**
  - **361 (34%) Self expandable**
- **Analysis of events depending on timing of stroke**

Nombela-Franco et al. Circulation. 2012 Dec 18;126(25):3041-53

Predictors of Early (30-Day) CVEs



Nombela-Franco et al. Circulation. 2012 Dec 18;126(25):3041-53

Predictors of Late CVEs (>30-day)

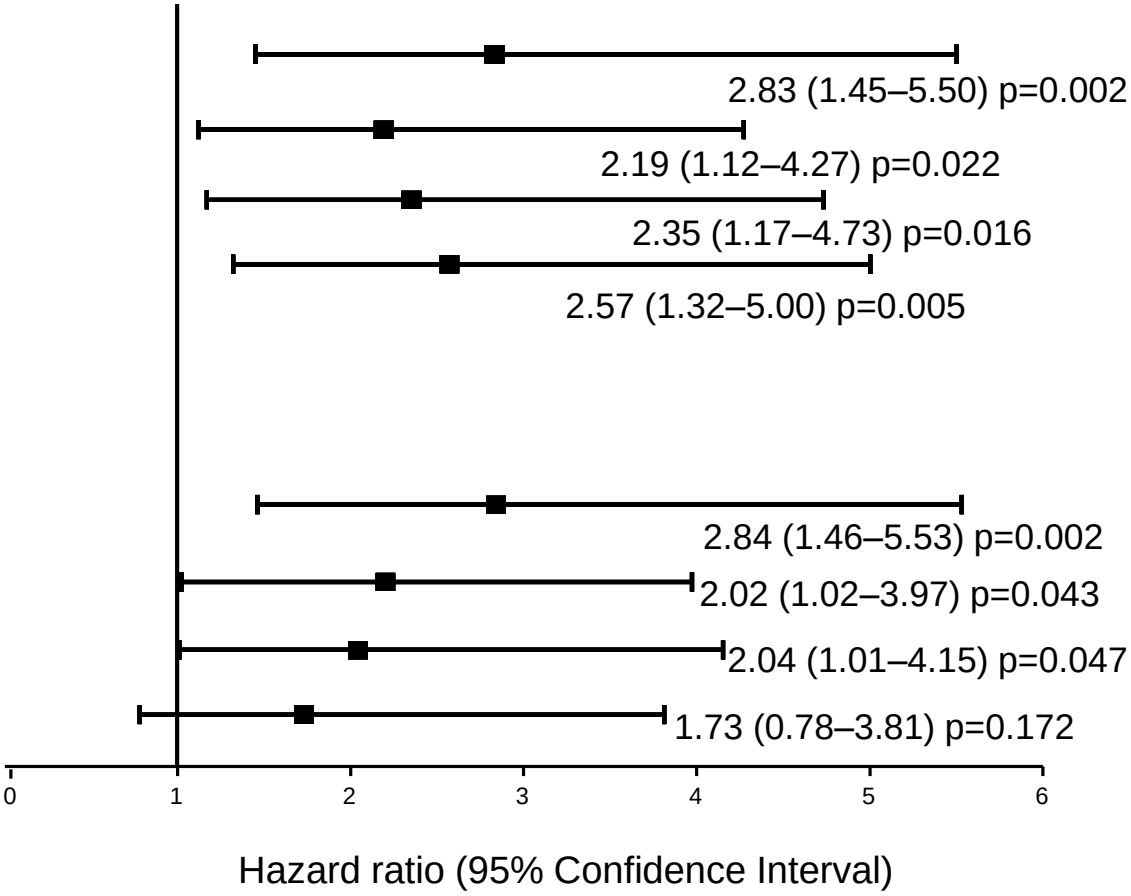
UNIVARIATE

Chronic atrial fibrillation

Peripheral vascular disease

Cerebrovascular disease

Anticoagulation treatment at hospital discharge



MULTIVARIATE

Chronic atrial fibrillation

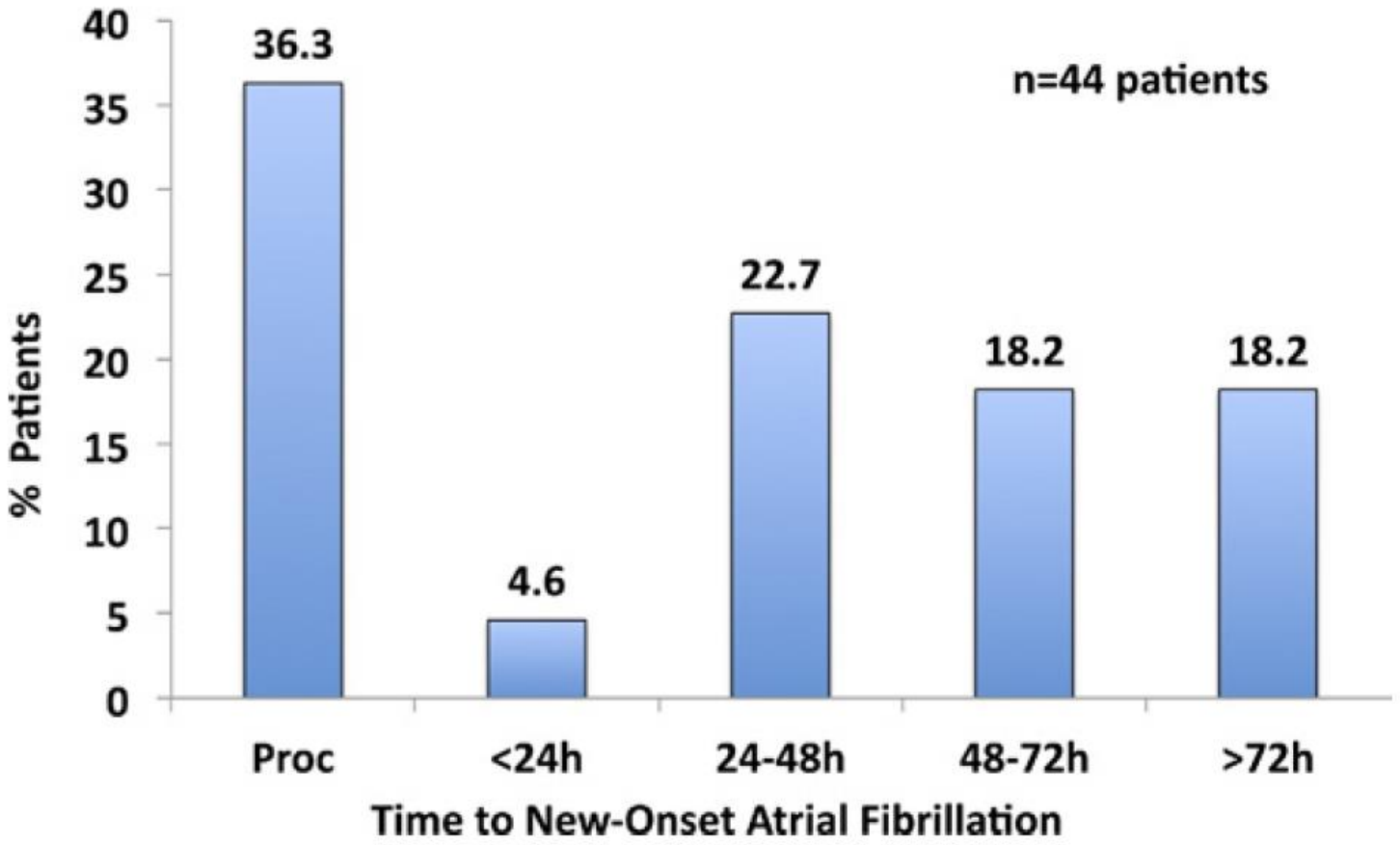
Peripheral vascular disease

Cerebrovascular disease

Anticoagulation treatment at hospital discharge

Nombela-Franco et al. Circulation. 2012 Dec 18;126(25):3041-53

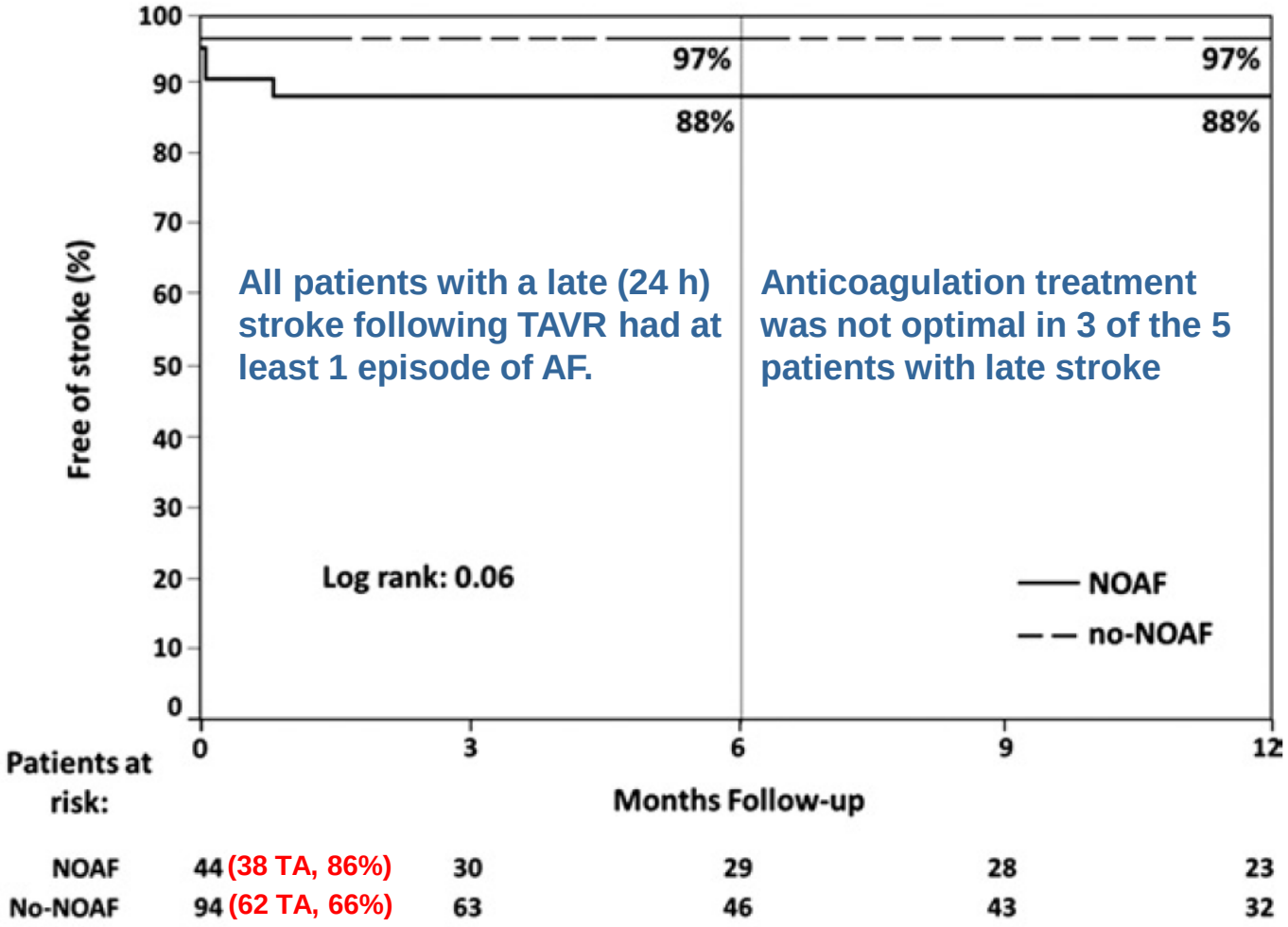
Timing of NOAF after TAVR



Predictors of NOAF were LA size > 27 mm/m^2 and TA approach

Amat-Santos et al, JACC 2012;59:178–88

New Onset AF after TAVR and Stroke



Amat-Santos et al, JACC 2012;59:178–88

Stroke

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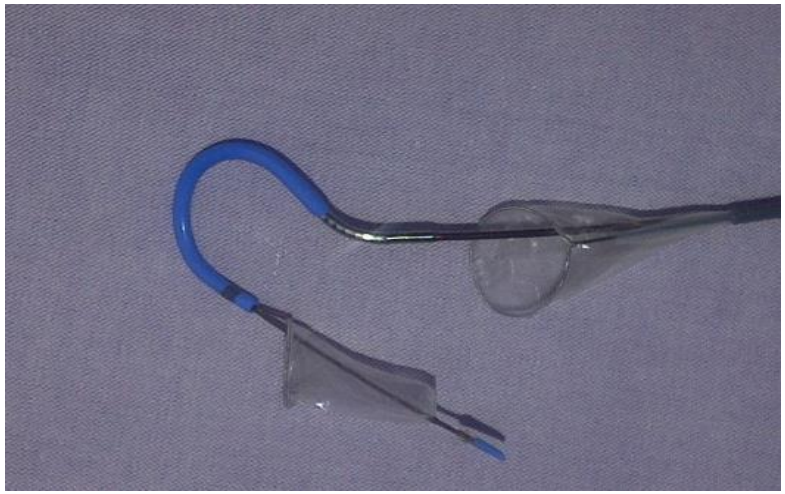
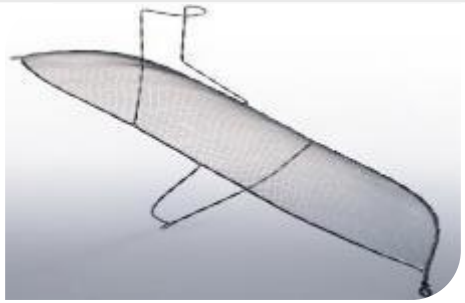
Stroke Prevention Measures

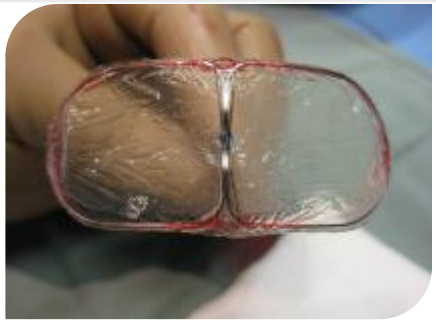
- Emboli prevention devices
  - Claret device - Sentinel Trial
    -- CLEAN TAVI
  - Embrella Device – ProTAVI
  - TriGaurd – DEFLECT 1
- Carotid pressure at the time of advancing the sheath
- Careful manipulations
- Minimize postdilations
- ? Pretreat carotid disease



Emboli Protection Devices

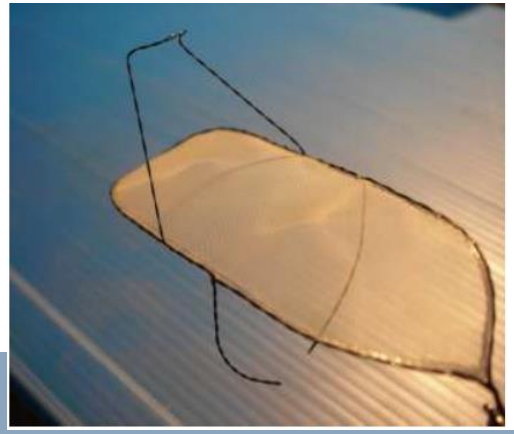
TriGuard™ Cerebral Protection Device	Edwards Embrella™ Embolic Deflector	Claret Sentinel™ Cerebral Protection System
Deflector	Deflector	**Filter capture**
9F (femoral)	6F (radial)	**6F (radial)**
240 micron pore size	100 micron pore size	**140 micron pore size**
Aortic arch position	Aortic arch position	**Brachiocephalic and LCC**
CE Marked	CE Marked	**CE Marked and Commercialized**

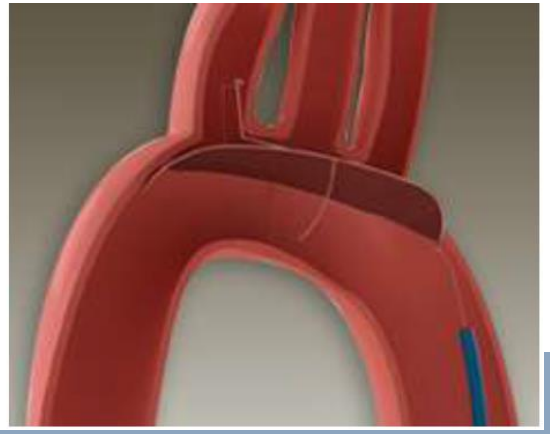




TriGuard - DEFLECT 1

Parameter	DEFLECT-I N=20	Historical Data N=150
Proportion of Patients with New Lesions	70%	76%
Number of New Lesions	5.1 (0 - 28)	4.4 (0 -39)
Average New Lesion Volume	0.12 (0 - 0.39) cm^3	0.34 cm^3
Max Single New Lesion Volume	0.39 cm^3	6.45 cm^3
Total New Lesion Volume	0.70 (0 – 3.94) cm^3	1.64 (0 – 70.3) cm^3





PROTAVI-C

euro PCR 2013

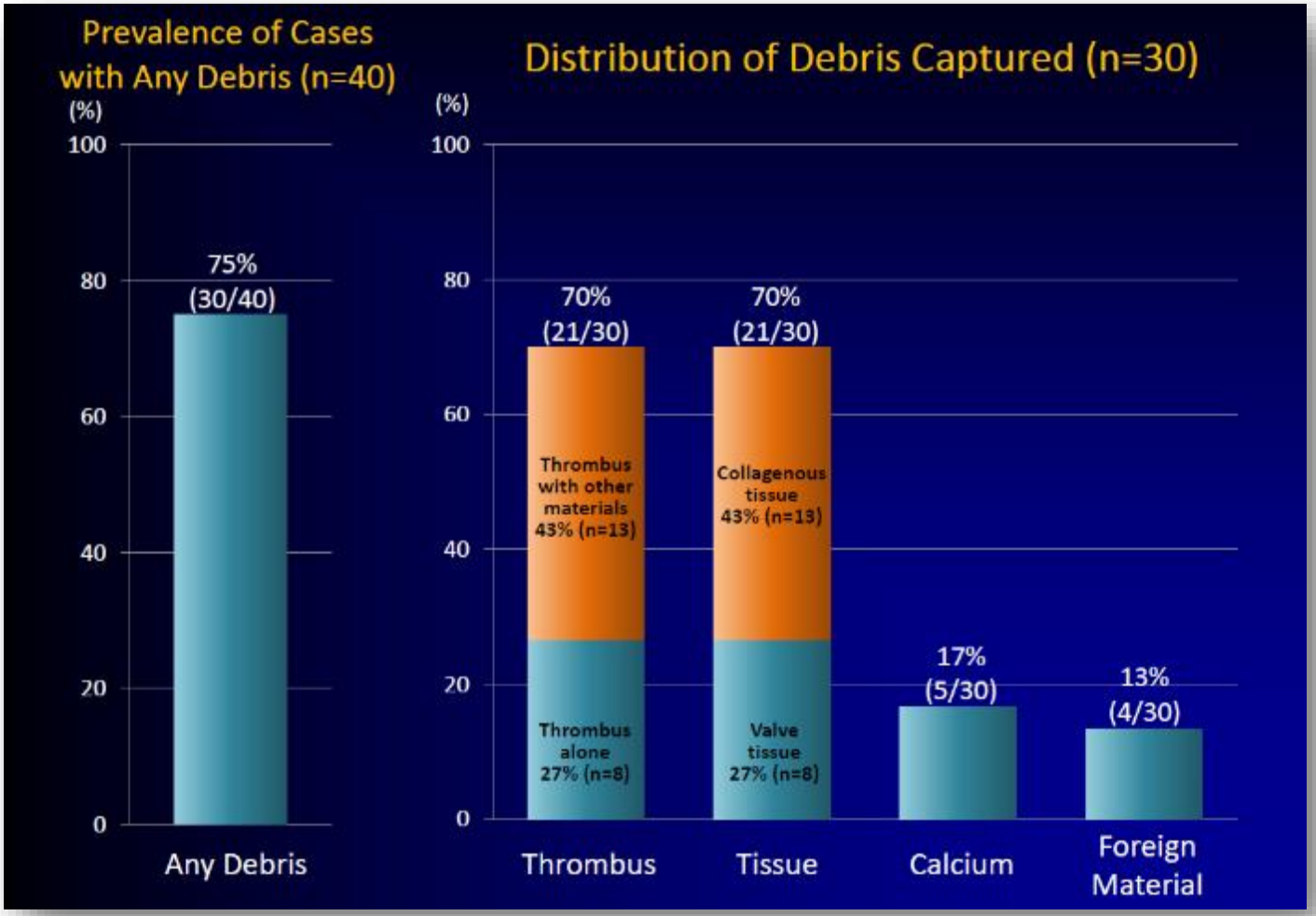
DW-MRI Data

	Roll-In (n=9)	Treatment TAVI + Embrella (n=24)	P Value
Time from TAVI procedure, days, median (min, max)	3 (1,7)	3 (1-7)	NA
Patients with new Lesions	9/9 (100%)	24/24 (100%)	NA
Total No. of lesions, n			
Anterior cerebral artery	1 (11%)	6 (25%)	0.642
Medial cerebral artery	9 (100%)	20 (83%)	0.555
Posterior cerebral artery	6 (67%)	16 (67%)	>.999
Cerebellum	8 (89%)	15 (63%)	0.217
Border zone	0	2 (8%)	>.999
Patients with single lesions	0	4 (17%)	>.999
Patients with multiple lesions	9 (100%)	20	0.555
Lesions per patient, median (min, max)	9 (2, 21)	7 (1, 70)	0.361
Lesion volume (mm^3), median (min, max)	69.4 (25.0, 210.6)	40.0 (10.8, 196.7)	0.897

PROTAVI-C

Presented by Dr. Rodes-Cabau

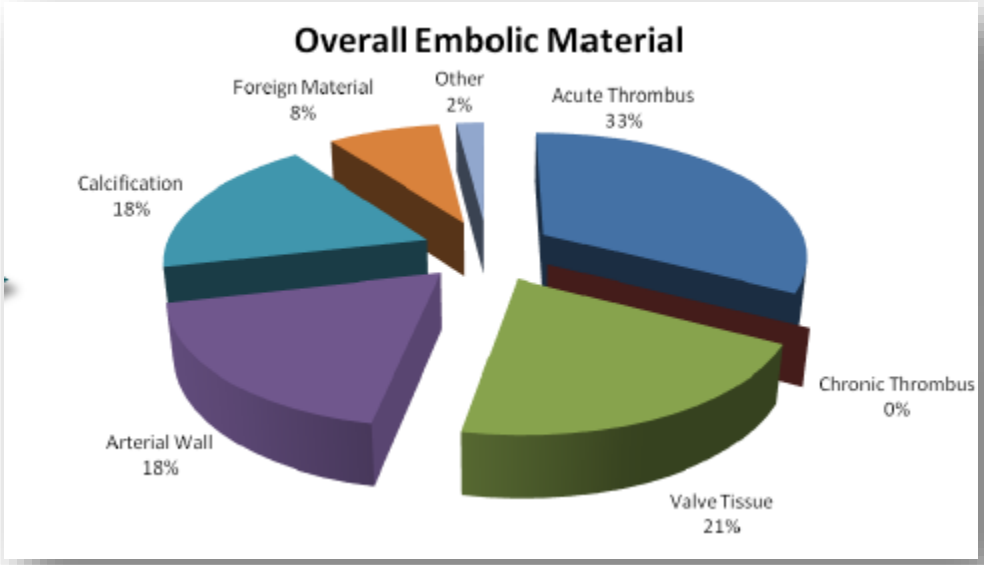
Histopathology - Claret Debris Capture

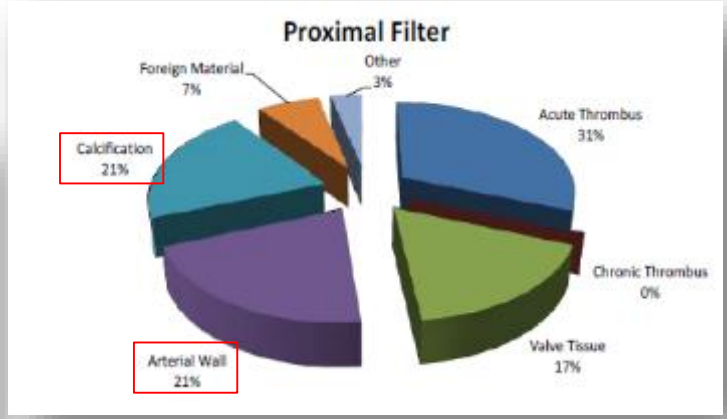


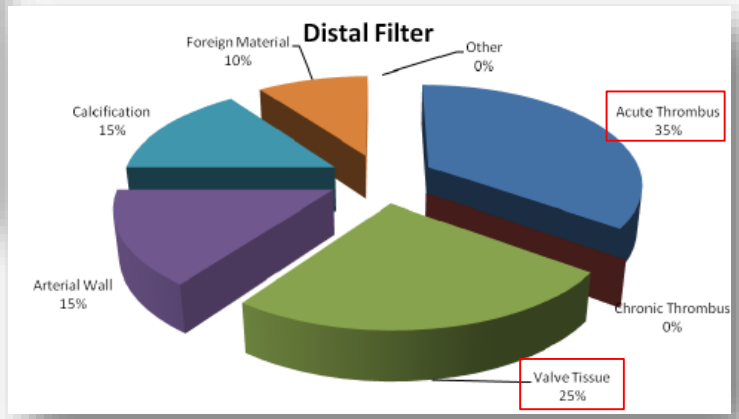
Van Mieghem et al, Circulation 2013;127:2194-2201
Debris analysis by Dr. Renu Virmani, CVPath Institute of Histopathology

Distribution & Analysis of Captured Debris

St. Georg Klinik, Germany & CVPath Institute, USA



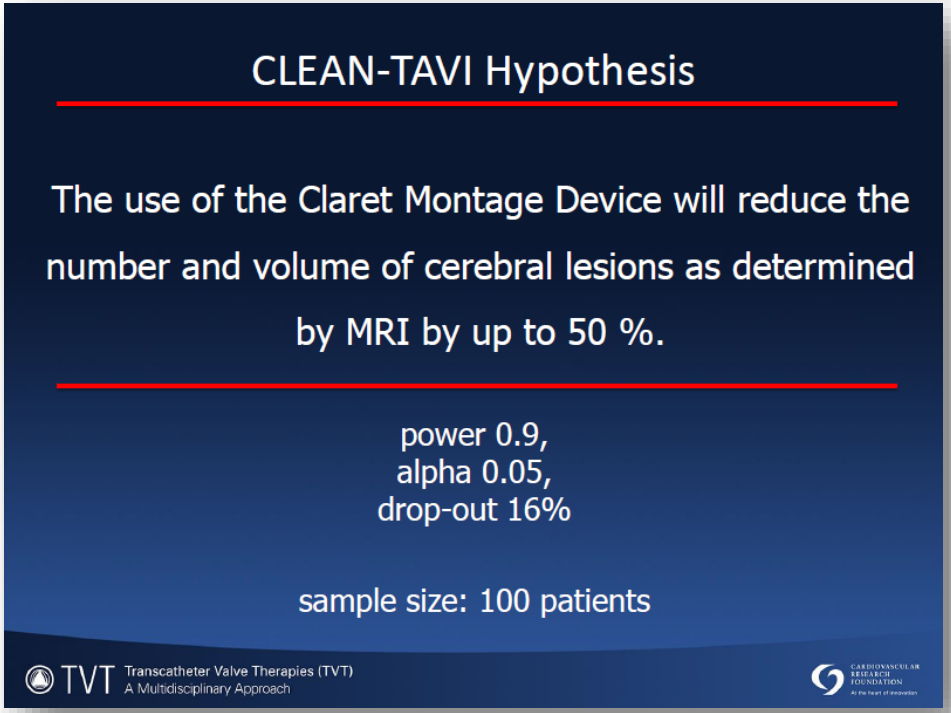


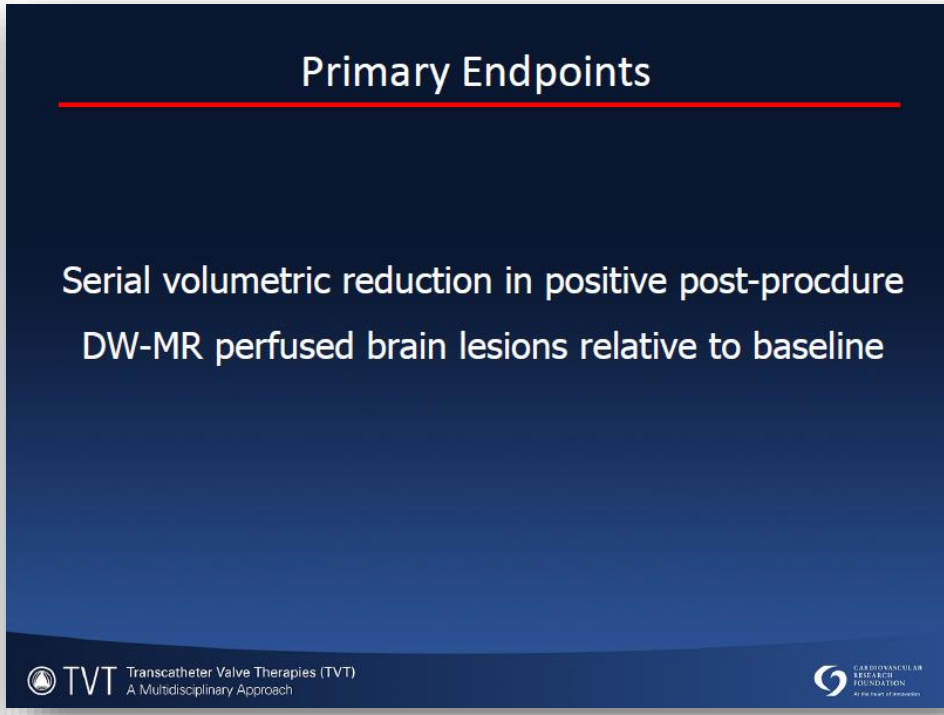


N= 10 Patients (20 Filters)

Dr. Renu Virmani, & Dr Elena Ladich CV Path
Data courtesy of Dr. Ulrich Schäfer and Dr. Christian Freker, St. Georg Klinik Asklepios, Hamburg, Germany

Clean-TAVI Study





- ***Statistically-powered: 100 patients randomized 1:1***
- ***Serial 3 Tesla MRI: Baseline, 2-days, 7-days, 1-month & 1-year***
- ***Medtronic CoreValve used exclusively***
- ***Presented at TCT on Saturday 13th 11am LBCT session***
- ***Data Showed decrease in volume, number of emboli with decrease in ataxia.***

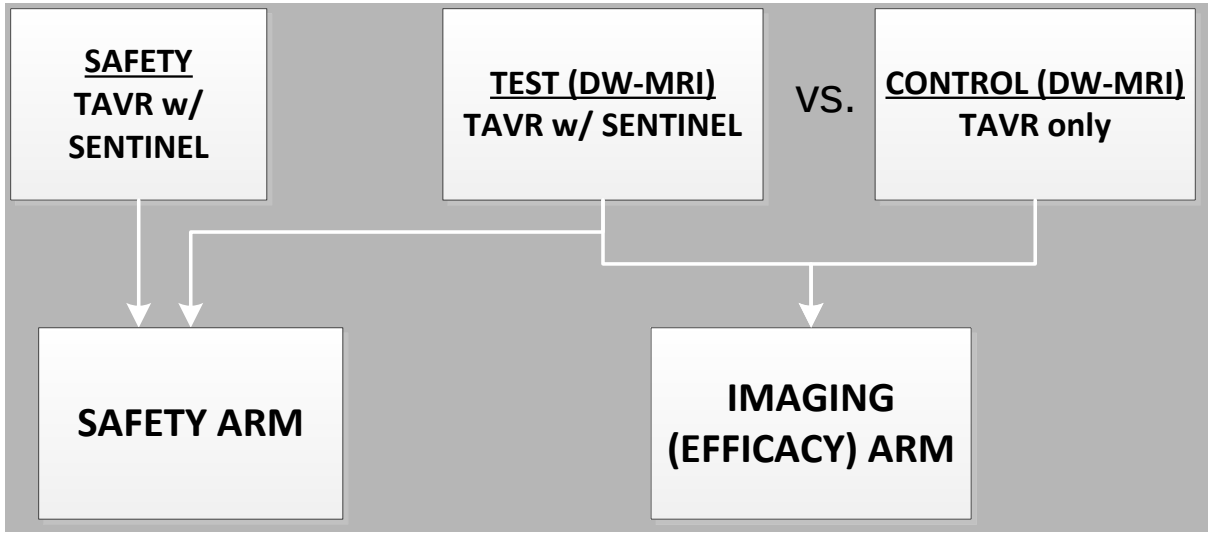
Courtesy of Prof Axel Linke, MD

US IDE Sentinel Study Summary

- **Title**
  - **Cerebral Protection in Transcatheter Aortic Valve Replacement Th SENTINEL Study**
- **Study Objective**
  - **Assess the safety and efficacy of the Claret Medical Sentinel Cerebral Protection System for embolic protection during Transcatheter Aortic Valve Replacement (TAVR) compared to TAVI standard of care (without embolic protection)**
- **Study Population**
  - **Subjects with severe symptomatic calcified native aortic valve stenosis who meet the commercially approved indications for TAVR with the Edwards SAPIEN THV or XT (if approved)**
- **Number of Centers**
  - **Up to 15 clinical study centers**

IDE Study Design - Overview

- Prospective, multicenter, blinded, randomized controlled trial
- 284 subjects randomized into a three-arm study
- Enrollment at up to 15 centers in the United States



Implication

- Stroke prevention will help to move to lower risk patients
- It may be an advantage rather than disadvantage for TAVR compared to SAVR (similar to PCI compared to CABG)