Transcatheter Aortic Valve Implantation

Stroke: etiology and prevention

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Disclosure Statement of Financial Interest

I, Corrado Tamburino, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation

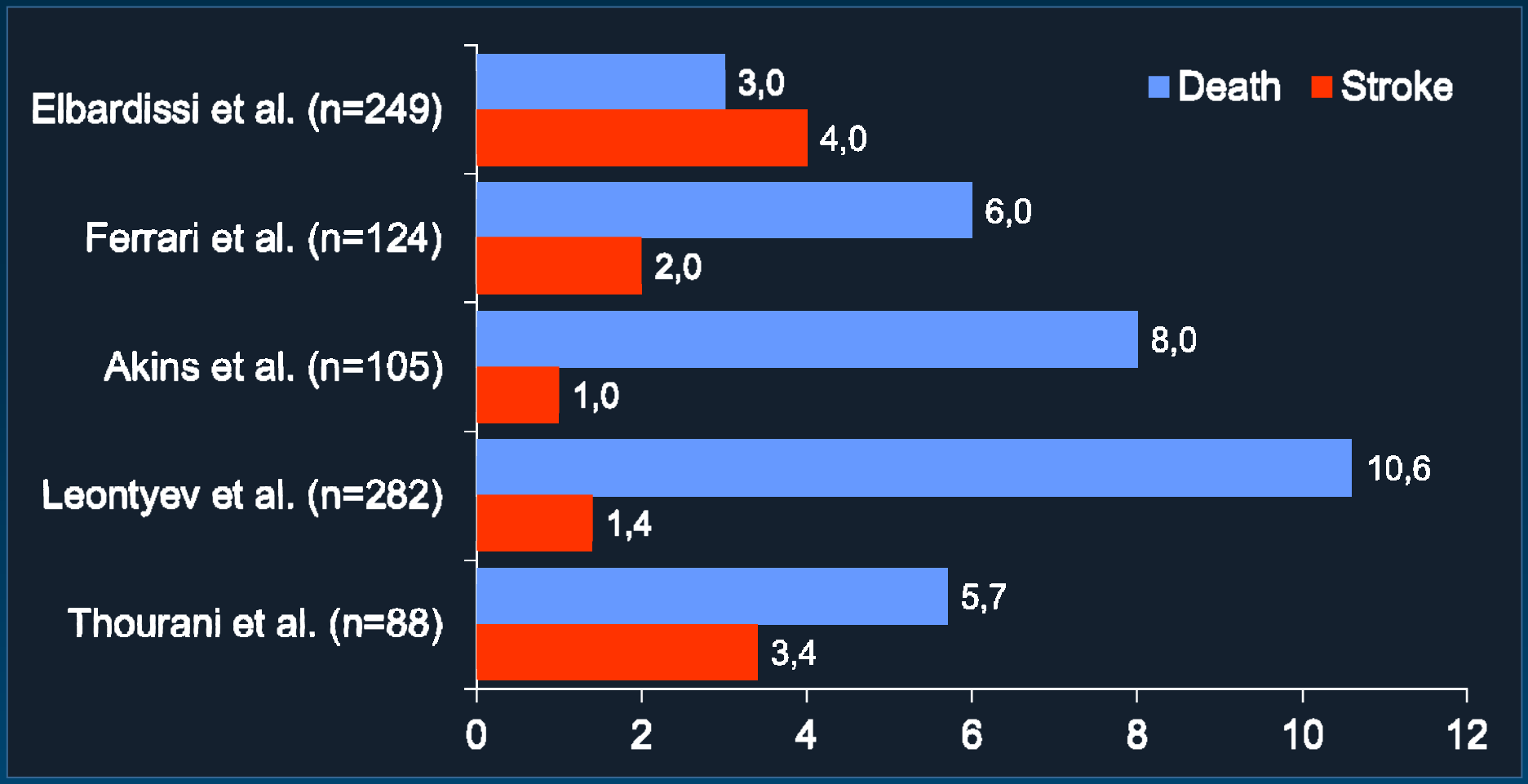
Stroke & TAVI

Background

- **Stroke is a potential major complication of SAVR, TAVI, and balloon aortic valvuloplasty;**
- **Although it is rare, stroke significantly affects survival and quality of life;**
- **In PARTNER, increased neurologic events associated with TAVI have raised concerns;**
- **Stroke etiology is still under debate, particularly when it occurs far from the procedure.**

Stroke

Perioperative stroke after cardiac surgery



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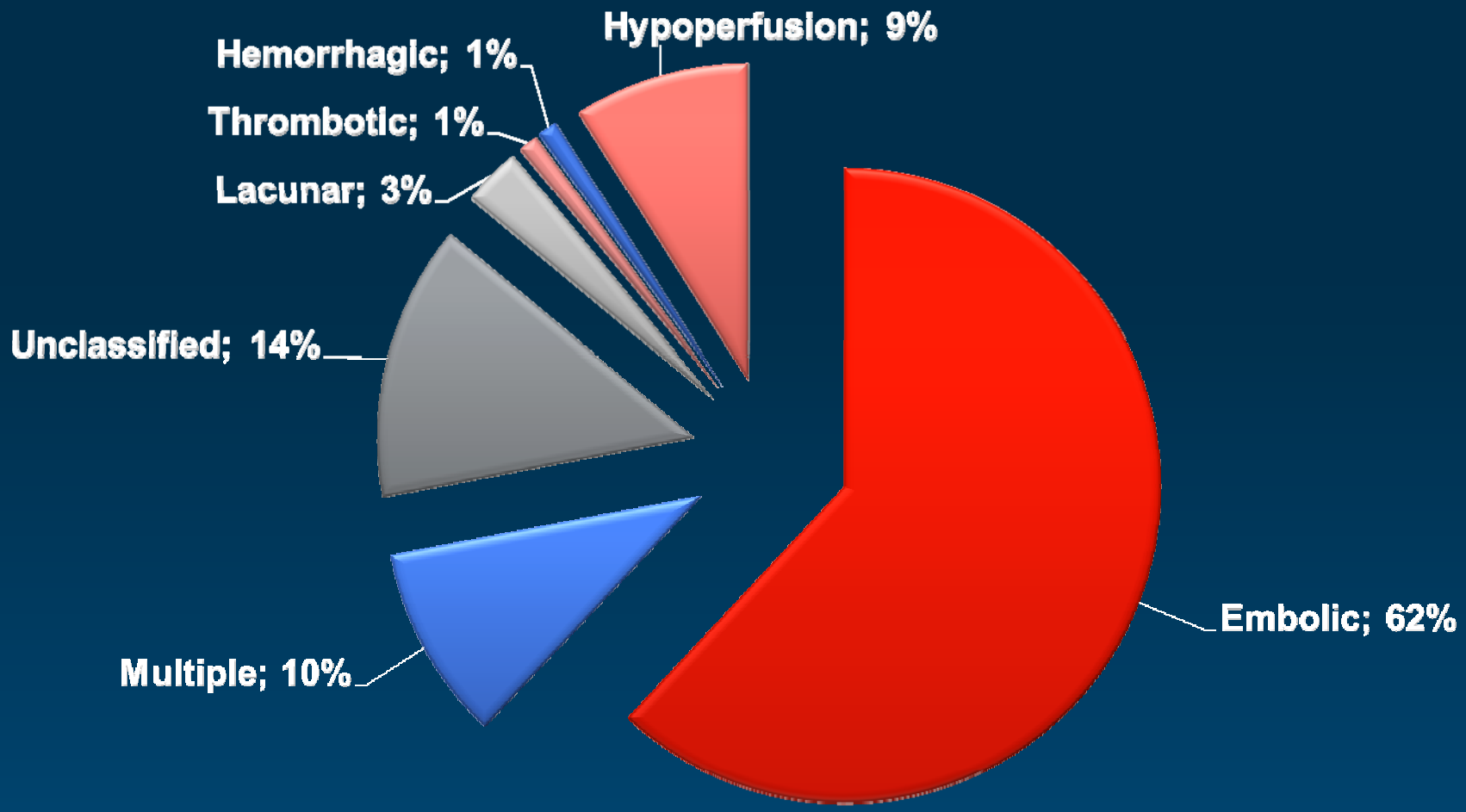
In-hospital outcomes
> 80 years of age

Stroke

Perioperative stroke after cardiac surgery



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Likosky et al. Stroke 2003

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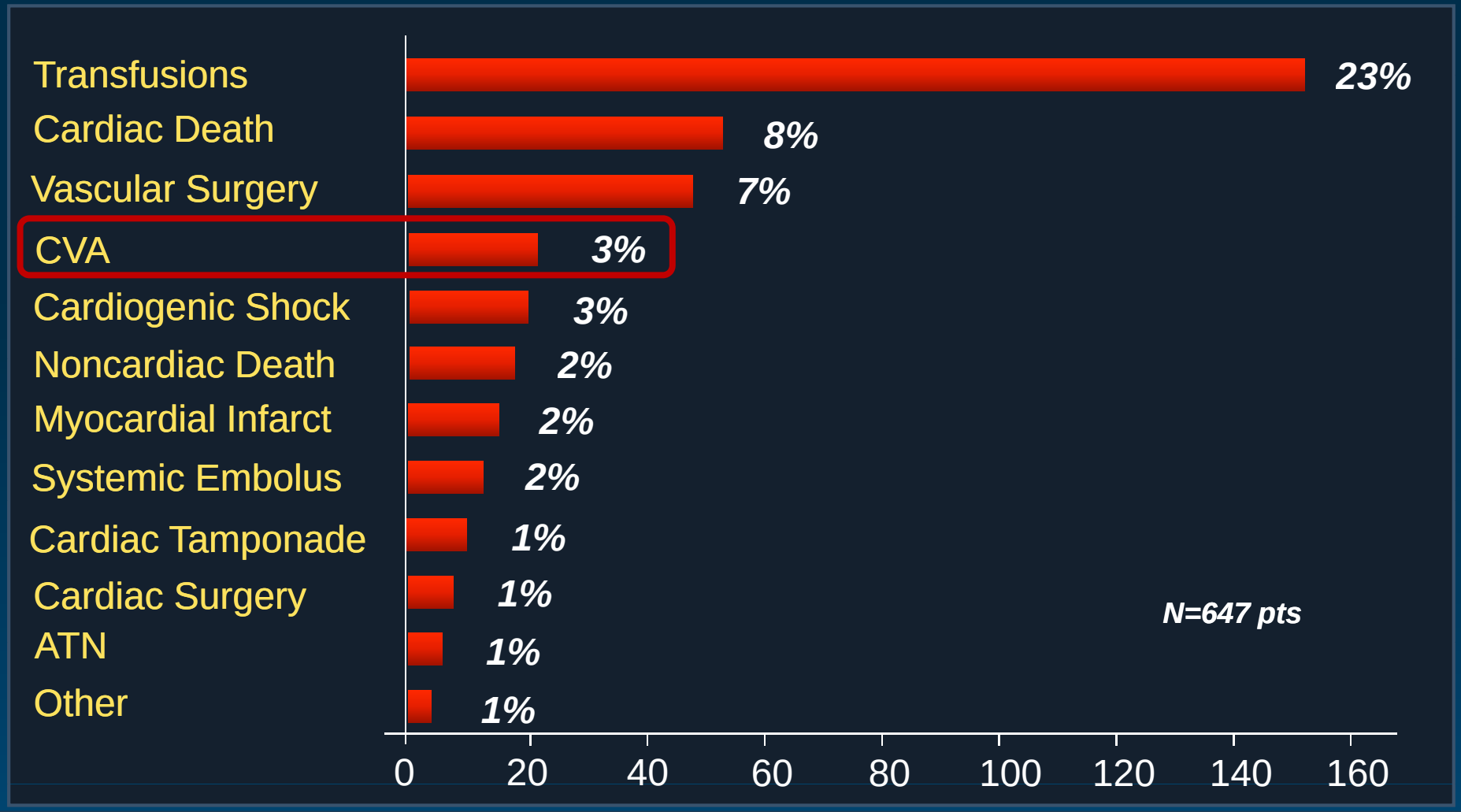
Stroke

Cerebrovascular accident after BAV



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NHLBI Balloon Valvuloplasty Registry Participants, Circulation1991;84:2383-2397

Stroke

Cerebrovascular accident after BAV

Serious Adverse Event	47 (15.6%)
Intraprocedural death, n (%)	79.1±33.6
Stroke, n (%)	6 (1.9%)
Coronary occlusion/dissection, n (%)	2 (0.7%)
Moderate-severe aortic regurgitation, n (%)	4 (1.3%)
Tamponade, n (%)	1 (0.3%)
Permanent pacemaker, n (%)	3 (0.9%)
Serious vascular complication requiring intervention, n (%)	21 (6.9%)
Perforation, n (%)	5 (1.6%)
Profound hypotension requiring resuscitation and intubation or cardioversion, n (%)	5 (1.6%)
Ischemic leg, n (%)	8 (2.6%)
Pseudoaneurysm, n (%)	6 (1.9%)
Arterial-venous fistula, n (%)	2 (0.7%)

Ben-Dor. et al, JACC: Cardiovasc Interv 2010

Table 3 VARC Definition of Stroke

Stroke diagnostic criteria
1. Rapid onset of a focal or global neurological deficit with at least 1 of the following: change in level of consciousness, hemiplegia, hemiparesis, numbness or sensory loss affecting one side of the body, dysphasia or aphasia, hemianopia, amaurosis fugax, or other neurological signs or symptoms consistent with stroke
2. Duration of a focal or global neurological deficit ≥24 h; OR <24 h, if therapeutic intervention(s) were performed (e.g., thrombolytic therapy or intracranial angioplasty); OR available neuroimaging documents a new hemorrhage or infarct; OR the neurological deficit results in death
3. No other readily identifiable nonstroke cause for the clinical presentation (e.g., brain tumor, trauma, infection, hypoglycemia, peripheral lesion, pharmacological influences)*
4. Confirmation of the diagnosis by at least 1 of the following:
Neurology or neurosurgical specialist
Neuroimaging procedure (MR or CT scan or cerebral angiography)
Lumbar puncture (i.e., spinal fluid analysis diagnostic of intracranial hemorrhage)
Stroke definitions
Transient ischemic attack:
New focal neurological deficit with rapid symptom resolution (usually 1–2 h), always within 24 h
Neuroimaging without tissue injury
Stroke: (diagnosis as above, preferably with positive neuroimaging study)
Minor—modified Rankin score <2 at 30 and 90 days†
Major—modified Rankin score ≥2 at 30 and 90 days

Stroke

Cerebrovascular accident after TAVI

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIALS

Transcatheter Aortic-Valve Implantation — At What Price?

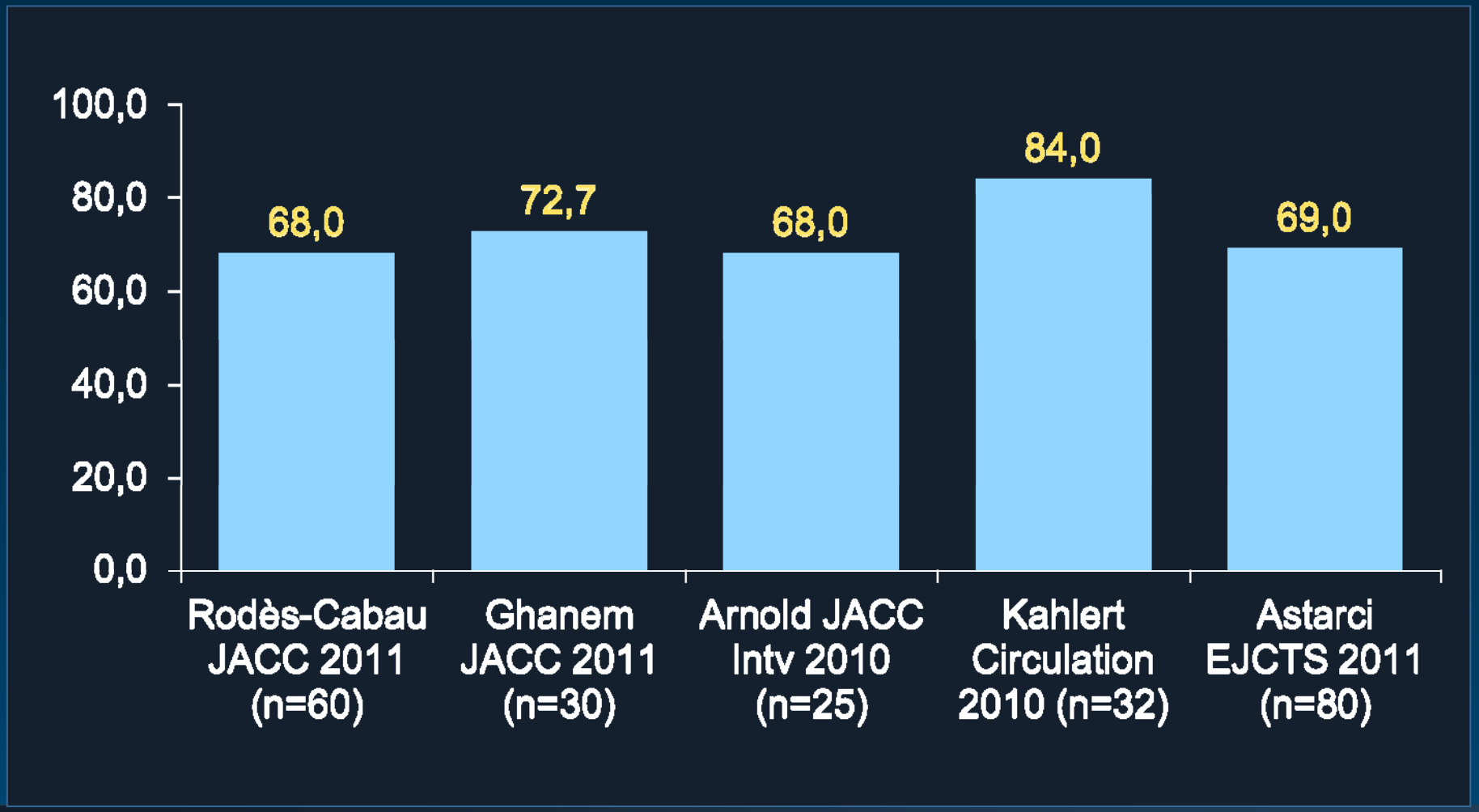
Hartzell V. Schaff, M.D.

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

Silent CVE post-TAVI

RMN new cerebral ischemic lesions



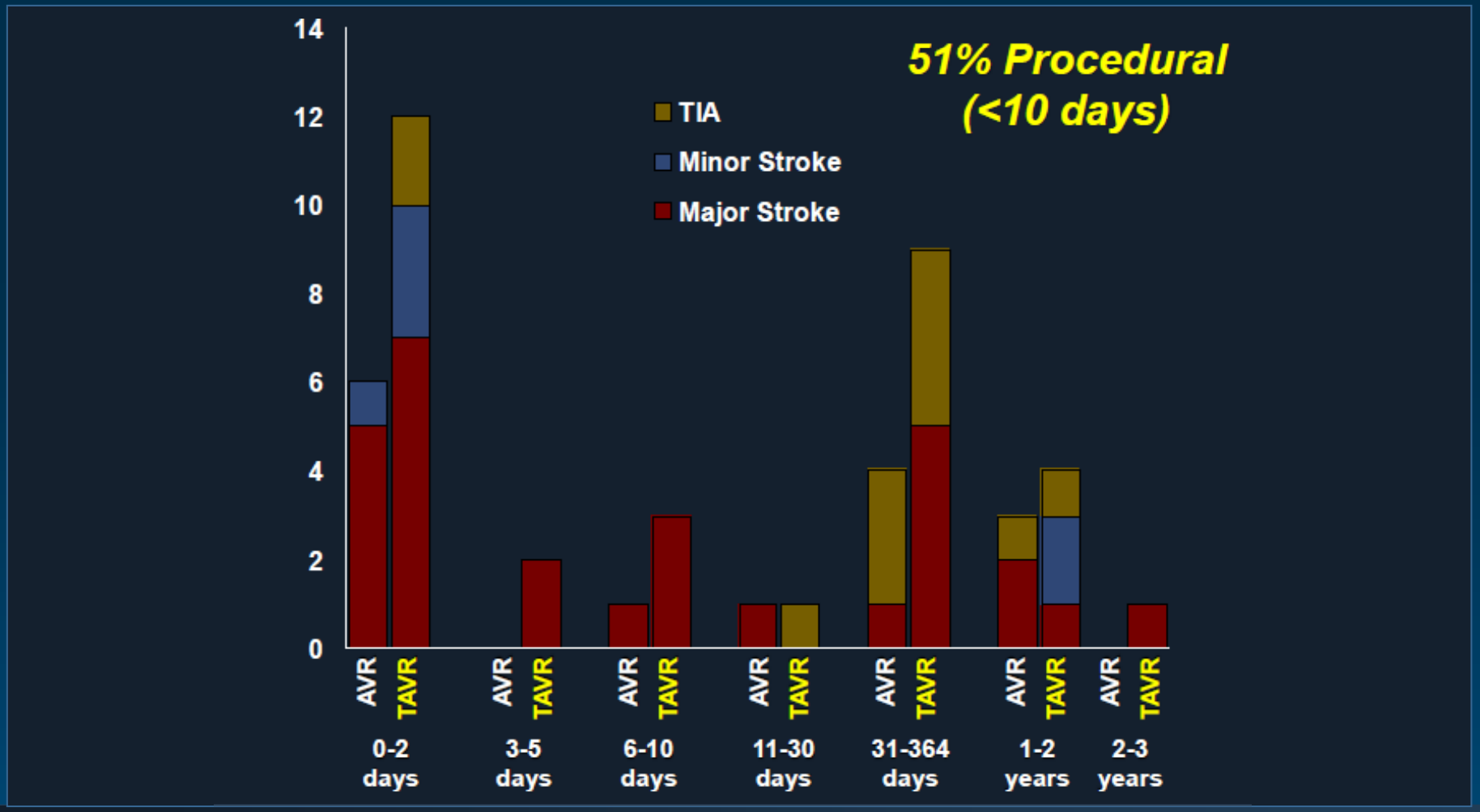
PARTNER Randomized Trial Cohort A

Neurological Events at 30 Days and 1 Year

Outcome	30 Days			1 Year		
	TAVR (N = 348)	AVR (N = 351)	p-value	TAVR (N = 348)	AVR (N = 351)	p-value
All Stroke or TIA – no. (%)	19 (5.5)	8 (2.4)	0.04	27 (8.3)	13 (4.3)	0.04
TIA – no. (%)	3 (0.9)	1 (0.3)	0.33	7 (2.3)	4 (1.5)	0.47
All Stroke – no. (%)	16 (4.6)	8 (2.4)	0.12	20 (6.0)	10 (3.2)	0.08
Major Stroke – no. (%)	13 (3.8)	7 (2.1)	0.20	17 (5.1)	8 (2.4)	0.07
Minor Stroke – no. (%)	3 (0.9)	1 (0.3)	0.34	3 (0.9)	2 (0.7)	0.84
Death/major stroke – no. (%)	24 (6.9)	28 (8.2)	0.52	92 (26.5)	93 (28.0)	0.68

PARTNER Randomized Trial Cohort A

Primary Endpoint: All-Cause Mortality at 1-Year



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Leon MB, TCT 2011

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Stroke after TAVI

High-Risk Period for CVE

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A High-Risk Period for Cerebrovascular Events Exists After Transcatheter Aortic Valve Implantation

CME

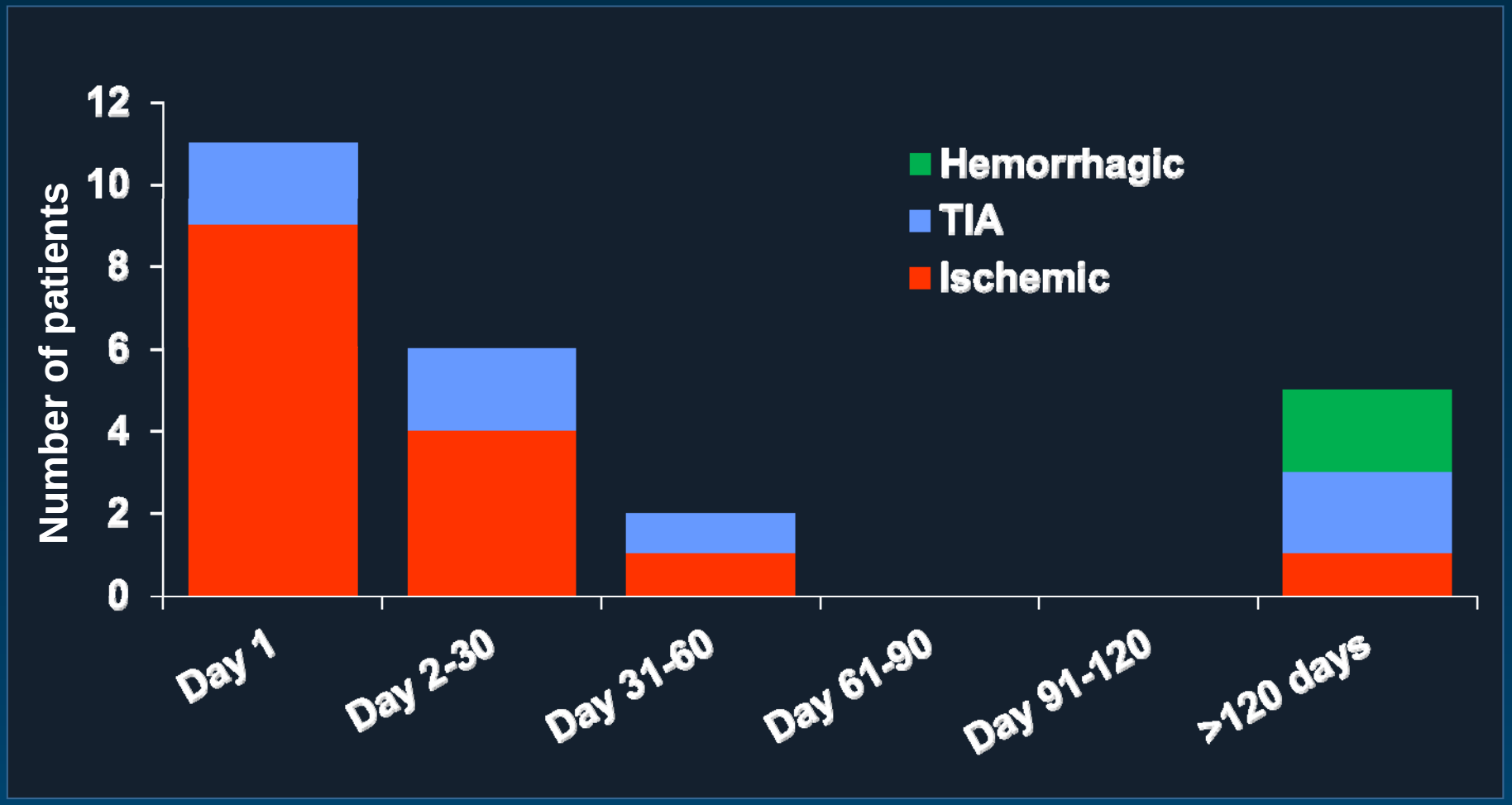
Edgar L. W. Tay, MD, Ronen Gurvitch, MD, Namal Wijesinghe, MD, Fabian Nielispach, MD, David Wood, MD, Anson Cheung, MD, Jian Ye, MD, Samuel V. Lichtenstein, MD, Ronald Carere, MD, Christopher Thompson, MD, John G. Webb, MD

British Columbia, Vancouver, Canada

Tay et al, JACC Cardiovasc Interv 2011

Stroke after TAVI

High-Risk Period for CVE



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Tay et al, JACC Cardiovasc Interv 2011

Stroke incidence from TAVI Registries

Table 2 Stroke After TAVR According to Access Site and Device Type: Major Published Data

First Author (Ref. #)	Type of Study	n	STS	EuroSCORE	Follow-Up, Months	Death		Stroke	
						30-day	1-yr	30-day	1-yr
Edwards Sapien: TF									
Lefevre et al. (25)	Registry	61	11.3%	25.7%	12	8.2%	21.3%	3.3%	7.0%
Eltchaninoff et al. (21)	Registry	95	17.4%	25.6%	1	8.4%	—	4.2%	—
Himbert et al. (24)	Registry	51	15.0%	25.0%	12	8.0%*	19.0%	6.0%*	—
Rodes-Cabau et al. (22)	Registry	113	9.0%	—	24	9.5%	25.0%	3.0%	—
Thomas et al. (23)	Registry	463	—	14.5%	1	6.3%	18.9%	2.4%	—
Leon et al. (1)	RCT	179	11.2%	26.4%	12	5.0%	30.7%	6.7%†	10.6%†
Edwards Sapien: TA									
Walther et al. (26)								2.0%	5.0%
Svensson et al. (27)								5.0%	—
Lefevre et al. (25)								1.5%	10.3%
Eltchaninoff et al. (21)								2.8%	—
Himbert et al. (24)								0%*	—
Rodes-Cabau et al. (22)								1.7%	—
Thomas et al. (23)	Registry	575	—	16.3%	1	10.3%	27.9%‡	2.6%	—
Medtronic CoreValve: TF									
Grube et al. (29)	Registry	136	—	23.1%	12	12.5%	29.8%	4.4%	7.1%‡
Piazza et al. (31)	Registry	646	—	23.1%	1	8.0%	—	1.9%	—
Eltchaninoff et al. (21)	Registry	66	21.3%	24.7%	1	15.1%	—	4.5%	—
Petronio et al. (30)	Registry	460	—	19.4%	6	6.1%	11.4%	1.7%	—
Medtronic CoreValve: SC									
Eltchaninoff et al. (21)	Registry	12	21.0%	24.6%	1	8.3%	—	0%	—
Petronio et al. (30)	Registry	54	—	25.3%	6	0%	6.7%	1.9%	—
Zahn et al. (32)	Registry	697	—	20.5%	1	12.4%	—	2.8%*	—

30-day average → 2,9%
12-month average → 8,0%

Daneault et al. JACC 2011

New onset AF after TAVI

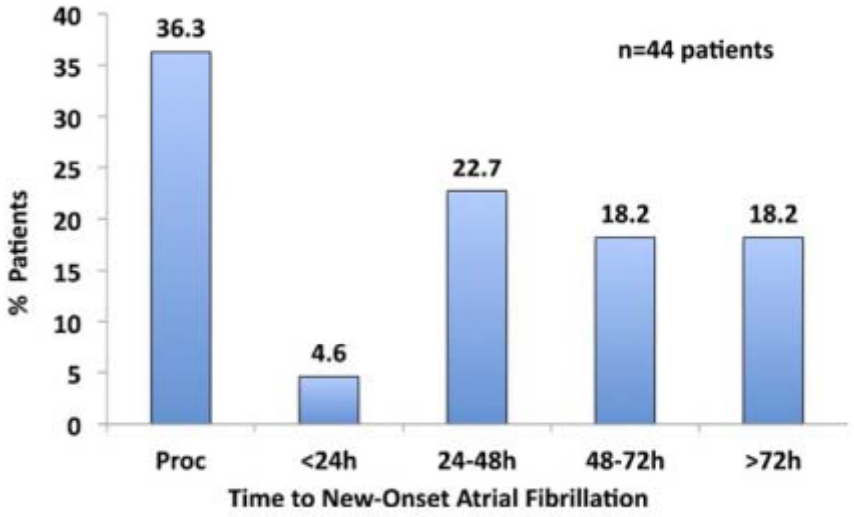
A potential source of CVE after TAVI?

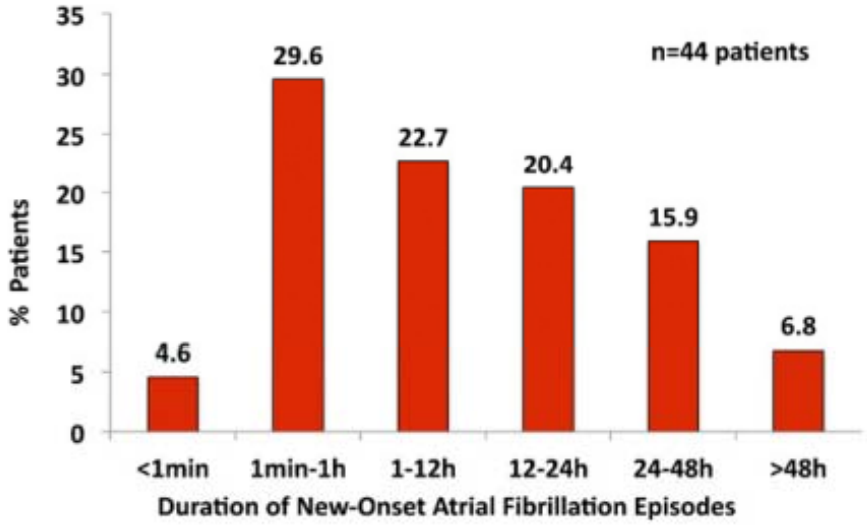
EXPEDITED PUBLICATIONS

Incidence, Predictive Factors, and Prognostic Value of New-Onset Atrial Fibrillation Following Transcatheter Aortic Valve Implantation

Ignacio J. Amat-Santos, MD, Josep Rodés-Cabau, MD, Marina Urena, MD, Robert DeLarochellière, MD, Daniel Doyle, MD, Rodrigo Bagur, MD, Jacques Villeneuve, MD, Mélanie Côté, MSc, Luis Nombela-Franco, MD, François Philippon, MD, Philippe Pibarot, DVM, PhD, Eric Dumont, MD

Quebec City, Quebec, Canada





Amat-Santos et al.JACC 2012

New onset AF after TAVI

A potential source of CVE after TAVI?

EXPEDITED PUBLICATIONS

Cumulative outcomes				
Cerebrovascular event	6 (13.6)	4 (4.3)	4.27 (1.07–17.09)	0.040
TIA	0	1 (1.1)	—	—
Stroke	6 (13.6)	3 (3.2)	4.32 (1.08–17.28)	0.039
Minor	3 (6.8)	1 (1.1)	6.39 (0.66–61.42)	0.11
Major	3 (6.8)	2 (2.1)	3.21 (0.54–19.23)	0.20
Fatal	0	0	—	—
Systemic embolism	1 (2.3)	0	—	—
Stroke or systemic embolism	7 (15.9)	3 (3.2)	5.00 (1.29–19.35)	0.020
Death	7 (15.9)	20 (21.3)	0.79 (0.33–1.86)	0.58
Cardiac	5 (11.4)	9 (9.6)	1.28 (0.43–3.82)	0.66
Noncardiac	2 (4.5)	11 (11.7)	0.39 (0.086–1.79)	0.23
Death or stroke	12 (27.3)	23 (24.5)	1.16 (0.58–2.35)	0.67

Proc <24h 24-48h 48-72h >72h — Time to New-Onset Atrial Fibrillation

<1min 1min-1h 1-12h 12-24h 24-48h >48h — Duration of New-Onset Atrial Fibrillation Episodes

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Amat-Santos et al.JACC 2012

Stroke during TAVI

Potential sources of embolism

- **Crossing the aortic valve**
- **Balloon valvuloplasty**
- **Navigation of delivery catheters through the aortic arch**
- **Valve deployment**

Stroke after TAVI

Transfemoral vs Transapical appoach

CLINICAL RESEARCH Interventional Cardiology

Cerebral Embolism Following Transcatheter Aortic Valve Implantation

Comparison of Transfemoral and Transapical Approaches

Josep Rodés-Cabau, MD,* Eric Dumont, MD,* Robert H. Boone, MD,† Eric Larose, MD,* Rodrigo Bagur, MD,* Ronen Gurvitch, MBBS,† Fernand Bédard, MD,‡ Daniel Doyle, MD,* Robert De Larochellière, MD,* Cleonie Jayasuria, MD,† Jacques Villeneuve, MD,* Alier Marrero, MD,§ Mélanie Côté, MSc,* Philippe Pibarot, PhD,* John G. Webb, MD†

Quebec City and Montreal, Quebec, and Vancouver, British Columbia, Canada

Rodès-Cabau. et al, JACC 2011

Stroke after TAVI

Transfemoral vs Transapical appoach

Variables	All patients (n=60)	Transfemoral (n=29)	Transapical (n=31)	P value
Patients with new lesions	41 (68)	19 (66)	22 (71)	0.78
Total number of lesions	251	83	168	
Lesions per patient	3 (2–8)	3 (1–7)	4 (2–9)	0.38
Patients with single lesion	10 (24)	5 (26)	5 (23)	1,00
Patients with multiple lesions	31 (76)	14 (74)	17 (77)	
Lesion size, cm				
<1	229 (91)	76 (92)	153 (91)	1,00
1-5	22 (9)	7 (8)	153 (91)	1,00
1-5	0	0	0	-
Time of post-procedural DW-MRI, days	4 (2-6)	4 (2-6)	5 (3-6)	0,37

Rodès-Cabau. et al, JACC 2011

Stroke during TAVI

Potential sources of embolism

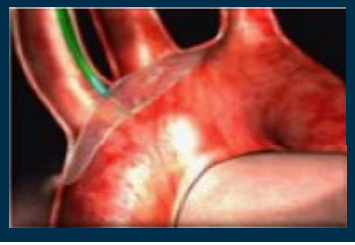
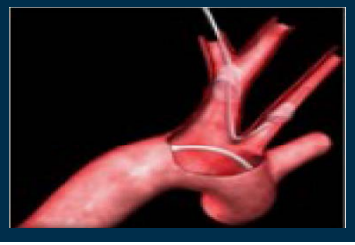
- **Crossing the aortic valve**
- **Balloon valvuloplasty**
- **Navigation of delivery catheters through the aortic arch (???)**
- **Valve deployment**

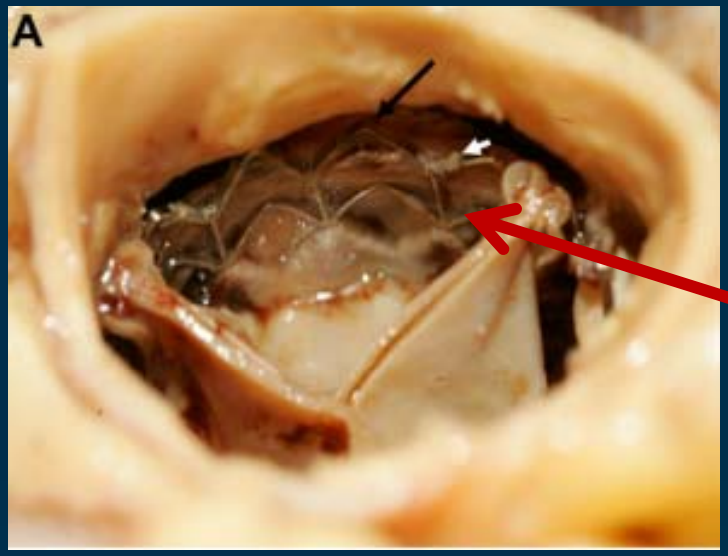
Stroke during TAVI

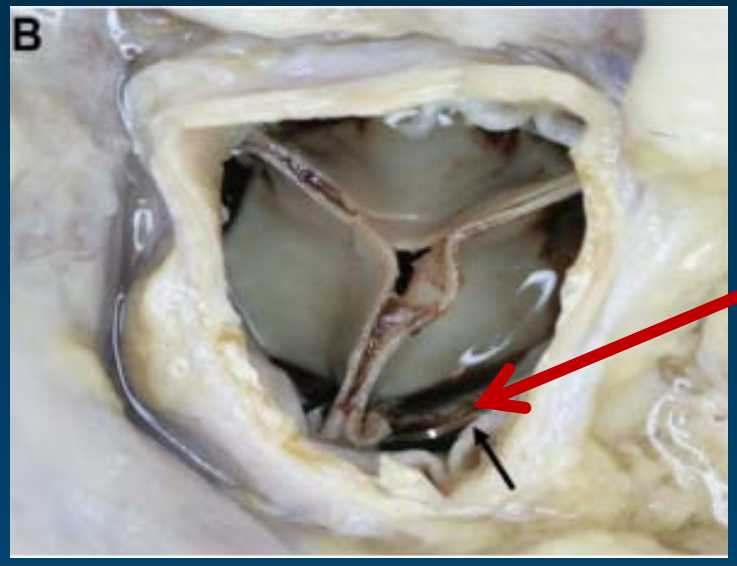
Aortic valve…lot of calcium!

Stroke during TAVI

SAT protection devices

Feature	Embrella	SMT	Claret Medical
			
Access	Radial	Femoral	Radial
Position	Aorta	Aorta	Brachiocephalic Left common carotid
Coverage area	Brachiocephalic & LCC	Brachiocephalic & LCC & LSA	Brachiocephalic & LCC
Mechanism	Deflection	Deflection	Deflection
Size	6 Fr	9 Fr	6 Fr
Pore Size	100 microns	~200 microns	140 microns
CE mark	Yes	No	No





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A High-Risk Period for Cerebrovascular Events Exists After Transcatheter Aortic Valve Implantation

CME

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British Columbia, Vancouver, Canada

Postmortem assessment Several stent struts are not endothelialized in these patients

Stroke after TAVI

Dual antiplatelet therapy, is it necessary!…

Dual Antiplatelet Therapy Versus Aspirin Alone in Patients Undergoing Transcatheter Aortic Valve Implantation

Gian Paolo Ussia, MD[a,b,*], Marilena Scarabelli, MD[a], Massimiliano Mulè, MD[a], Marco Barbanti, MD[a], Kunal Sarkar, MD[a], Valeria Cammalleri, MD[a], Sebastiano Immè, MD[a], Patrizia Aruta, MD[a], Anna Maria Pistritto, MD[a], Simona Gulino, MD[a], Wanda Deste, MD[a], Davide Capodanno, MD[a,b], and Corrado Tamburino, MD, PhD[a,b]

- **79 consecutive pts with TAVI**
- *Randomization 1:1, 40 DAPT vs 39 ASA alone*
- *300-mg loading dose of clopidogrel before TAVI followed by 3-month maintenance daily dose of 75 mg clopidogrel + ASA 100 mg lifelong* or ASA 100 mg alone
- **Primary end point: MACCE (death from any cause, MI, major stroke, urgent or emergency conversion to surgery, or life-threatening bleeding)**
- **No significant differences between the DAPT and ASA groups at both 30 days (13% vs 15%, p=0.71) and 6 months (18% vs 15%; p= 0.85)**

Ussia GP et al. Am J Cardiol 2012

Cardiovascular events & TAVI

Conclusions I

- **TAVI is associated with a high rate of new cerebral ischemic defects as evaluated by MRI**
- **Stroke rate at 30 days is ~3%**
- **Cerebral embolism during the TAVI procedure is probably multifactorial but seems to be mostly related to valve prosthesis positioning and implantation**

Cardiovascular events & TAVI

Conclusions II

- **Only about 50% of neurologic events occur within the 24 hours following the TAVI procedure**
- **Uncertainty about cause of stroke at follow-up**
- **Future studies will have to evaluate the potential usefulness of embolic protection devices as well as the optimal antithrombotic treatment following TAVI**