GRCI 2017
France

6 AU 8 DÉCEMBRE 2017
Novotel Paris Tour Eiffel

Passion Communication Education

Les risques neurologiques en cardiologie interventionnelle

GRCI

6 décembre 2017

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Institut Cœur Poumon - CHRU de Lille

Centre Hospitalier Régional Universitaire de Lille

DÉCLARATION DE LIENS D'INTÉRÊT AVEC LA PRÉSENTATION

Intervenant : Cédric Delhaye, Lille

☑ Je déclare les liens d'intérêt suivants :

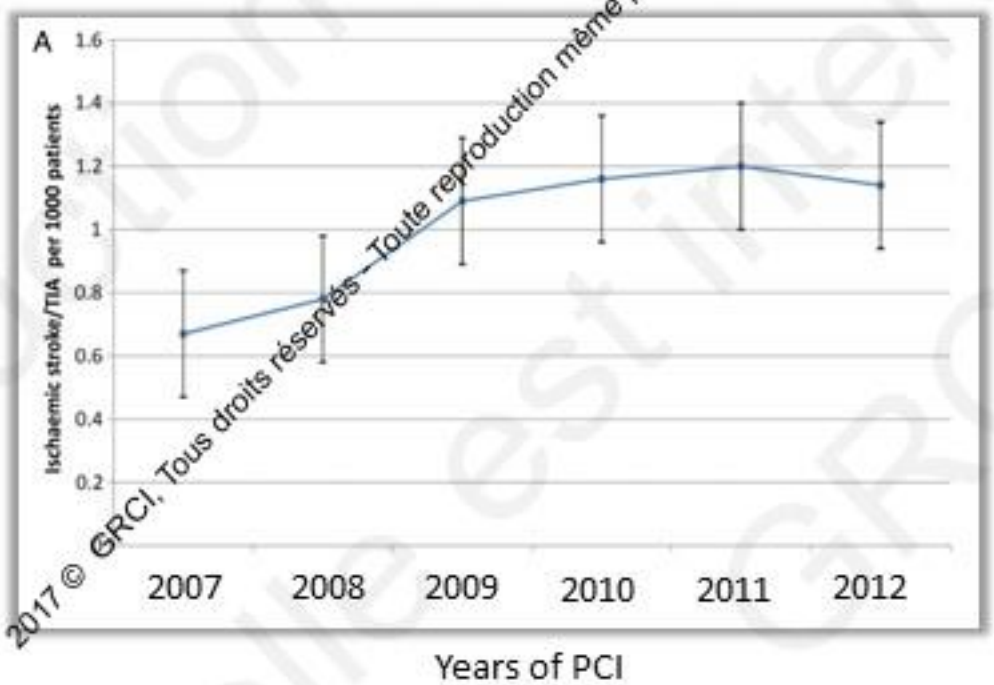
Consulting fees / Honoraria: Astrazeneca, Medtronic, MSD, Novartis

Grant / research Support: Medtronic

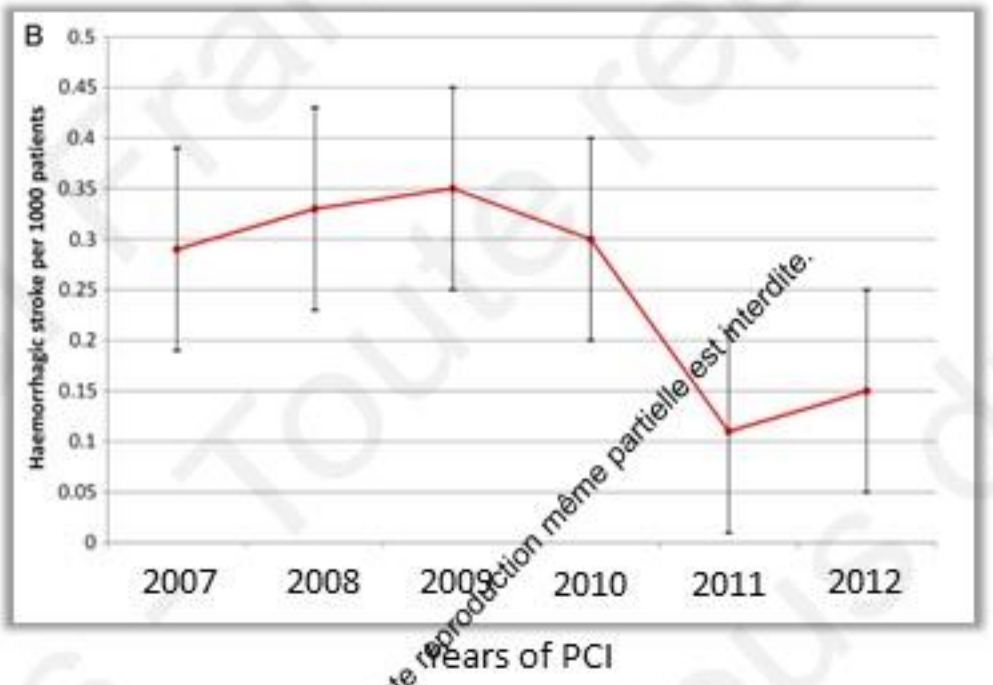
Incidence des AVC post-PCI

PCI British registry, 426 297 PCI patients ➔ 0.13%

In-hospital Ischaemic stroke / TIA = 0.1%



In-hospital haemorrhagic stroke = 0.03%



Kwok C S, European Heart Journal, 2015: 36, 1618–1628

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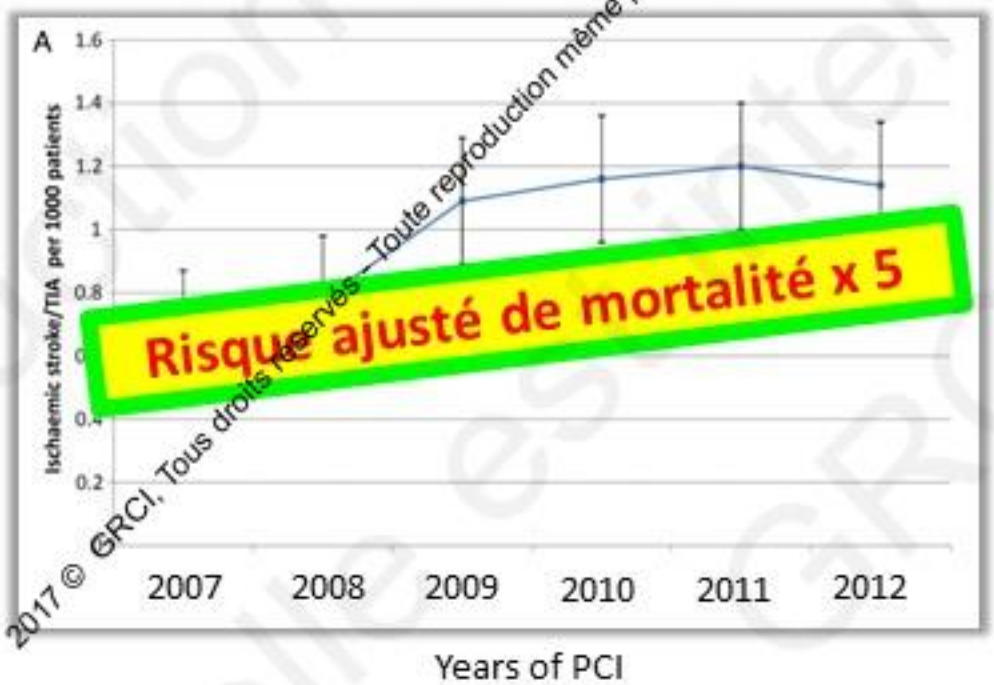

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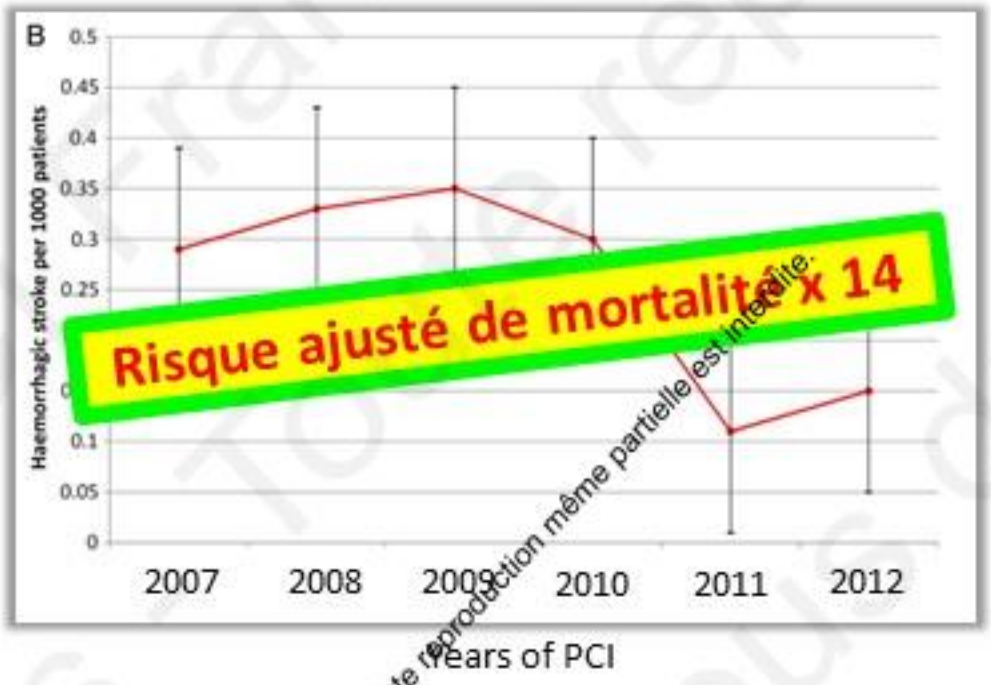


Kwok C S; European Heart Journal, 2015: 36, 1618–1628

Facteurs prédictifs des AVC post-PCI

PCI British registry, 426 297 PCI patients ➔ 0.13%

Independent predictors of ischaemic stroke / TIA

Variable	Odds ratio (95% CI)	*P*-value
Significant predictors of ischaemic stroke or transient ischaemic attack ($n = 238\,707$)		
Age	1.05 (1.04–1.06)	<0.001
Male gender	0.68 (0.53–0.87)	0.002
Previous stroke	1.88 (1.27–2.78)	0.002
Previous valvular heart disease	4.48 (2.87–7.00)	<0.001
Receipt of circulatory support	1.71 (1.03–2.84)	0.038
Thrombus aspiration	1.64 (1.19–2.27)	0.003
Diagnosis of NSTEMI	1.84 (1.30–2.61)	0.001
Diagnosis of STEMI	2.88 (1.92–4.33)	<0.001

Independent predictors of Haemorrhagic stroke

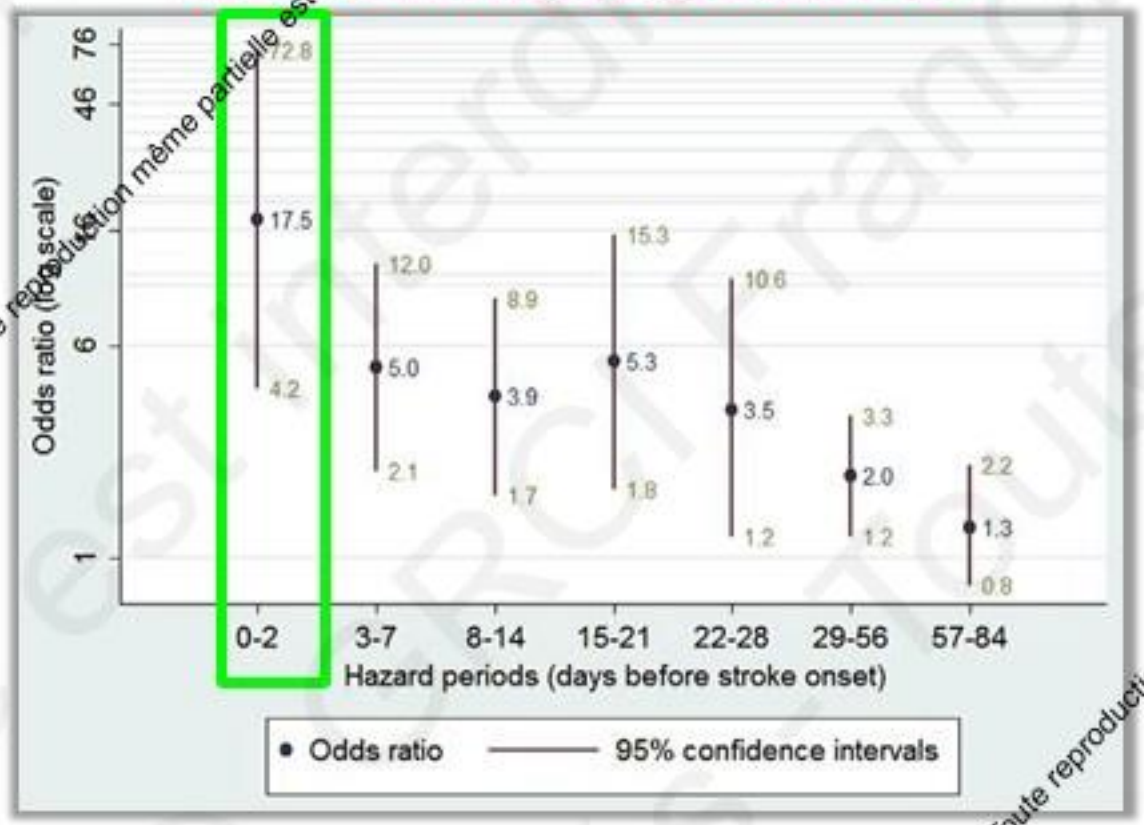
Variable	Odds ratio (95% CI)	*P*-value
Significant predictors of haemorrhagic stroke ($n = 225\,708$)		
Age	1.03 (1.00–1.05)	0.024
Previous valvular heart disease	21.30 (10.73–42.28)	<0.001
Diagnosis of NSTEMI	3.24 (1.19–8.79)	0.021
Diagnosis of STEMI	5.50 (1.91–15.85)	0.002
Warfarin use	4.47 (1.33–15.02)	0.015
Thrombolysis	4.02 (2.18–7.39)	<0.001

Kwok C S; European Heart Journal, 2015: 36, 1618–1628

Risque neurologique pas uniquement post-PCI immédiat

Norway Registry: 1 811 stroke post-PCI (2008- 2014)

RR of Ischemic stroke after PCI



Varmdal T, Am J Cardiol 2017; 119: 35-39

TAVI

Incidence des événements cérébro-vasculaires

FRANCE 2 registry

3191 TAVI from jan 2010 to dec 2011

CVE: 3.98%

55% major strokes

14.5% minor strokes

30.5% TIA

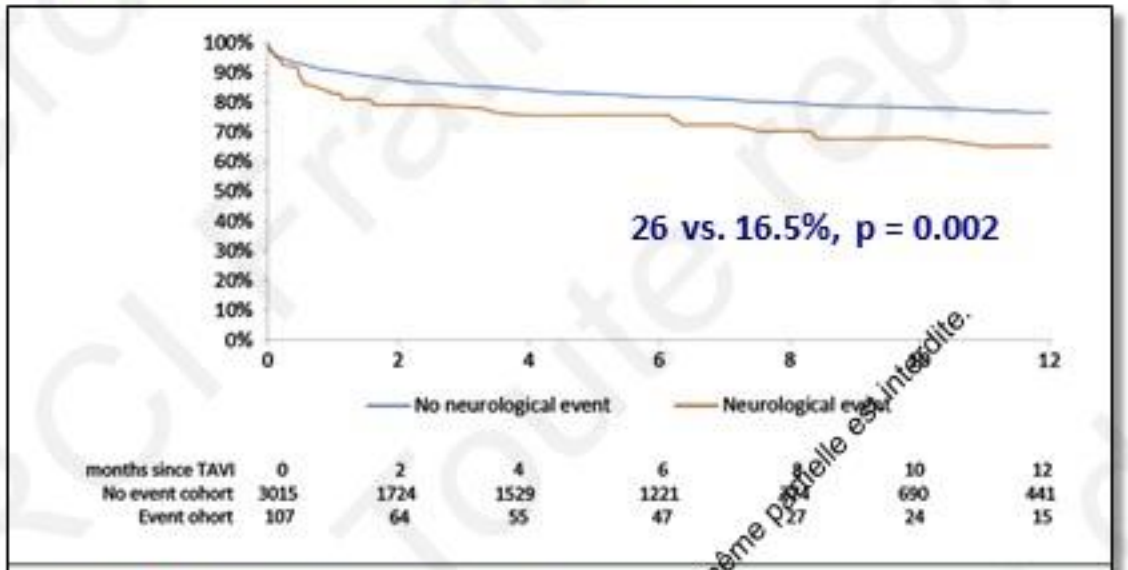


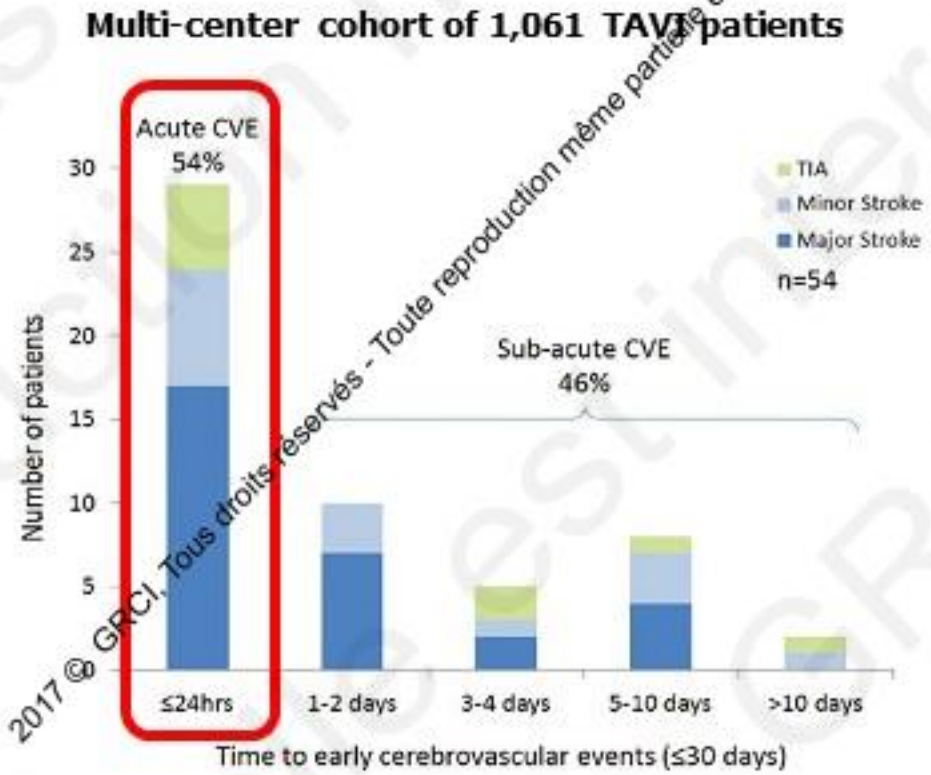
FIGURE 2 Kaplan-Meier Survival Curves

One-year survival of all-cause mortality in patients with and without a cerebrovascular event.

Tchetche et al. JACC Interv 2014

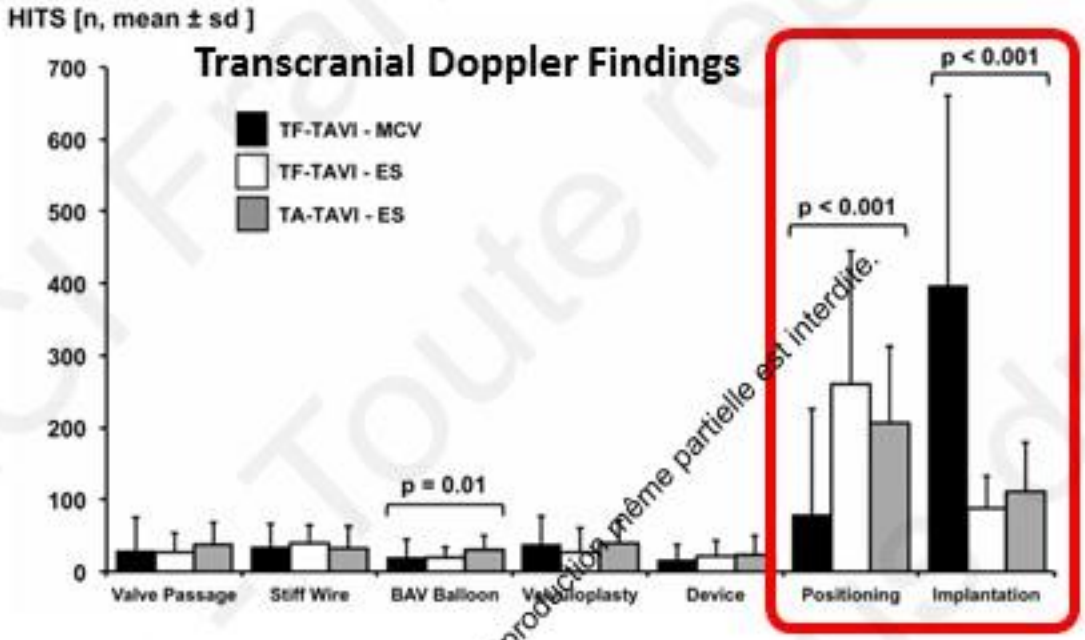
Timing & mécanismes des AVC

Essentiellement péri-procéduraux



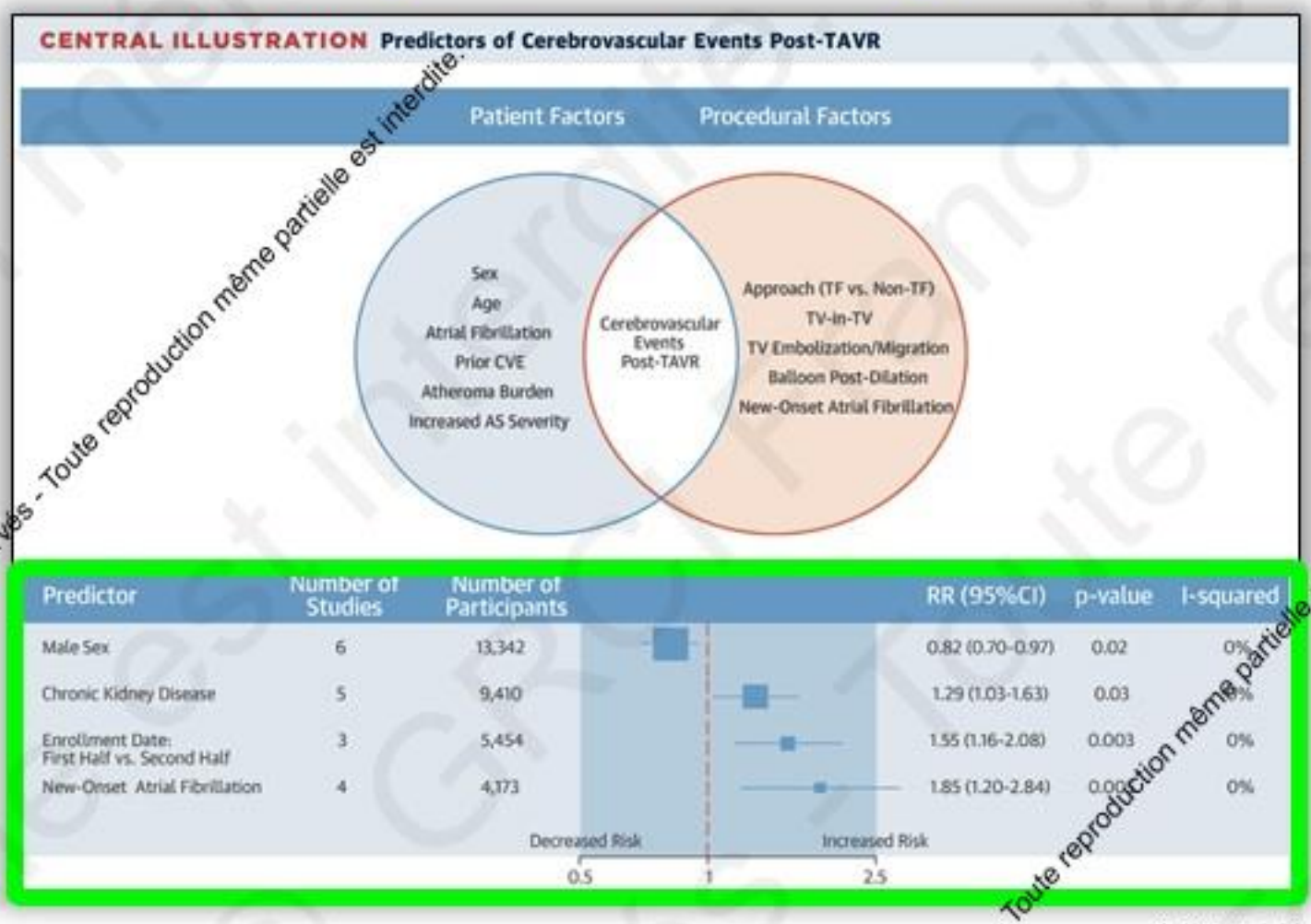
Nombela-Franco et al. Circulation 2012

Surtout au moment du positionnement et du déploiement



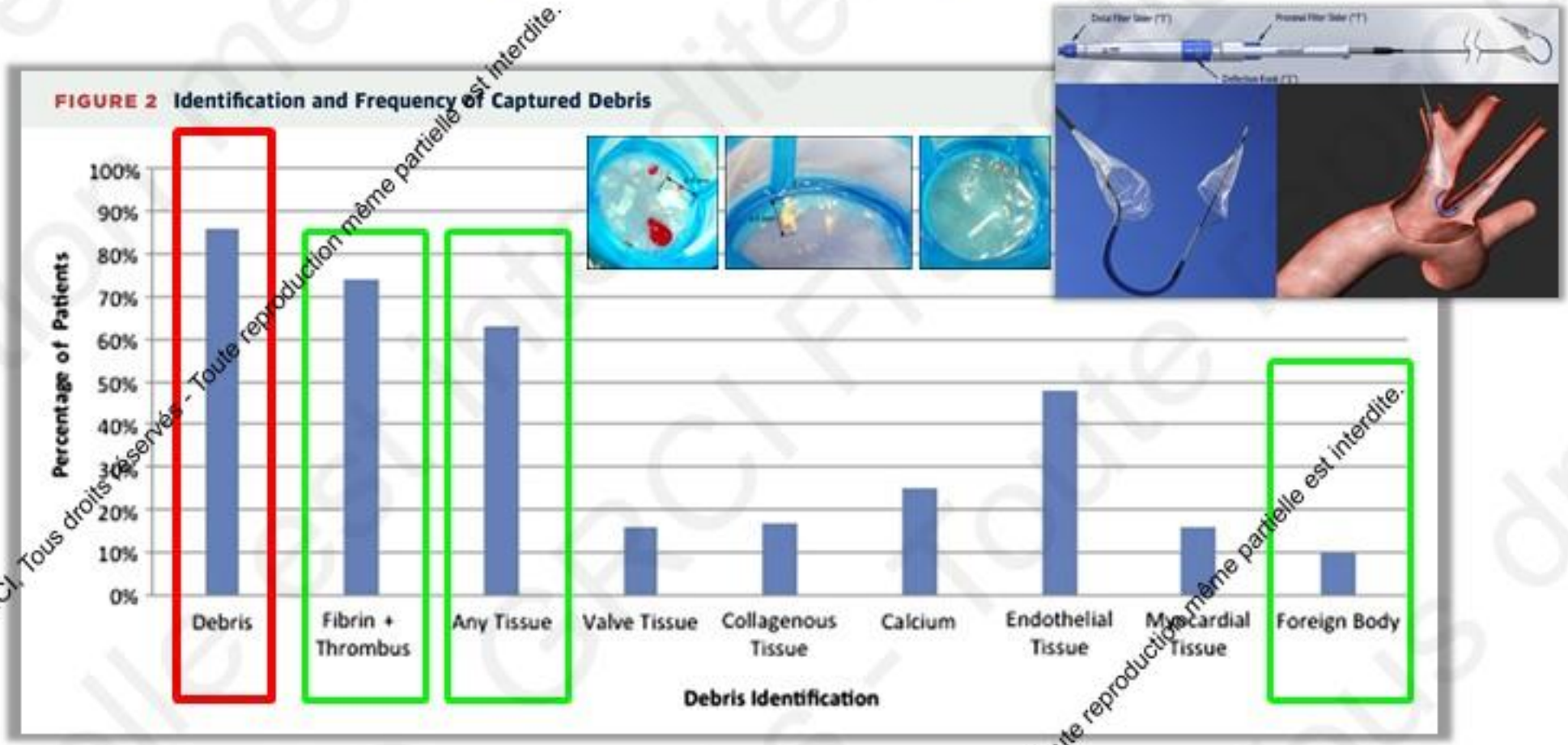
Kahlert P et al. Circulation 2012

Facteurs prédictifs d'AVC post-TAVI



Auffret et al. J Am Coll Cardiol. 2016; 68(7):673-84

Débris cérébraux post-TAVI: fréquence et nature ?



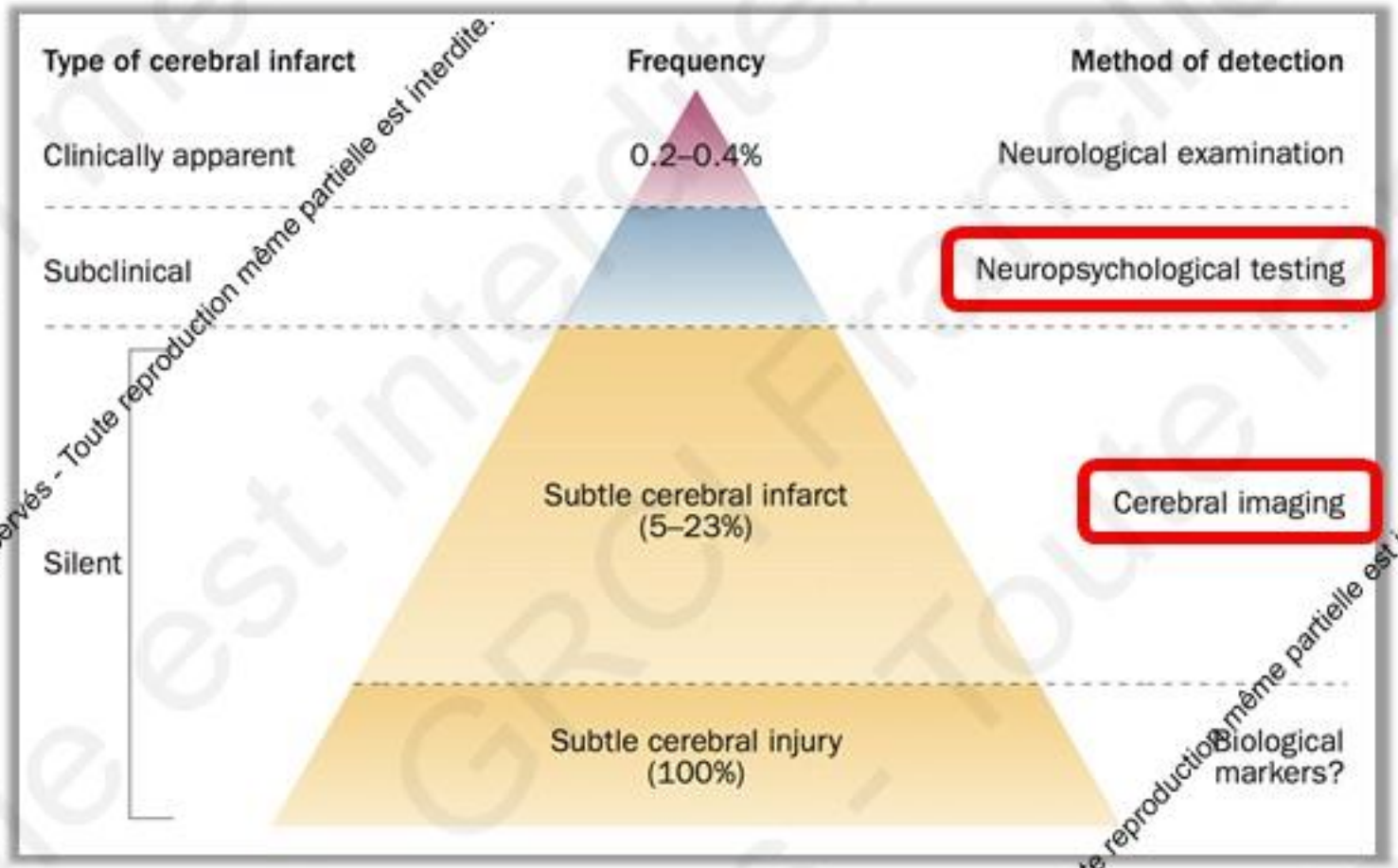
Van mieghen et al. J Am Coll Cardiol Intv 2015;8:718–24

Débris capturés par le système de neuroprotection Claret dans diverses procédures interventionnelles

Type of Procedure, Study, Center	# of Patients in Series	Any Debris	Valve Tissue	Arterial Wall Tissue	Calcification	Myocardium	Foreign Material	Organizing Thrombus	Acute Thrombus	Other
MitraClip[1] Aachen and Hamburg	n=14	93%	57%		0%	0%	79%	21%	79%	N/A
LAA Closure[2] AK St Georg (Hamburg)	n=5	100%	0%	40%	0%	0%	0%	80%	60%	N/A
TEVAR[3] West-German Heart and Vascular Center Essen	n=5	100%	40%	100%	20%	0%	100%	80%	100%	N/A
TEVAR[4] Imperial College, London	n=6	100%	33%	100%	0%	17%	50%	67%	100%	N/A
Valve in Valve[5] AK St Georg (Hamburg)	n=15	100%	60%	80%	73%	13%	27%	33%	100%	N/A

1. MitraClip study from Aachen and Hamburg. CVPath report on file at Claret Medical.
2. LAAO study from Hamburg. CVPath report on file at Claret Medical.
3. Janosi, et al. presented at LINC 2016. CVPath report on file at Claret Medical.
4. Grover, et al. presented at ISET 2016 and CVPath report on file at Claret Medical
5. Schmidt T, et al. *Heart* 2016;0:1–7

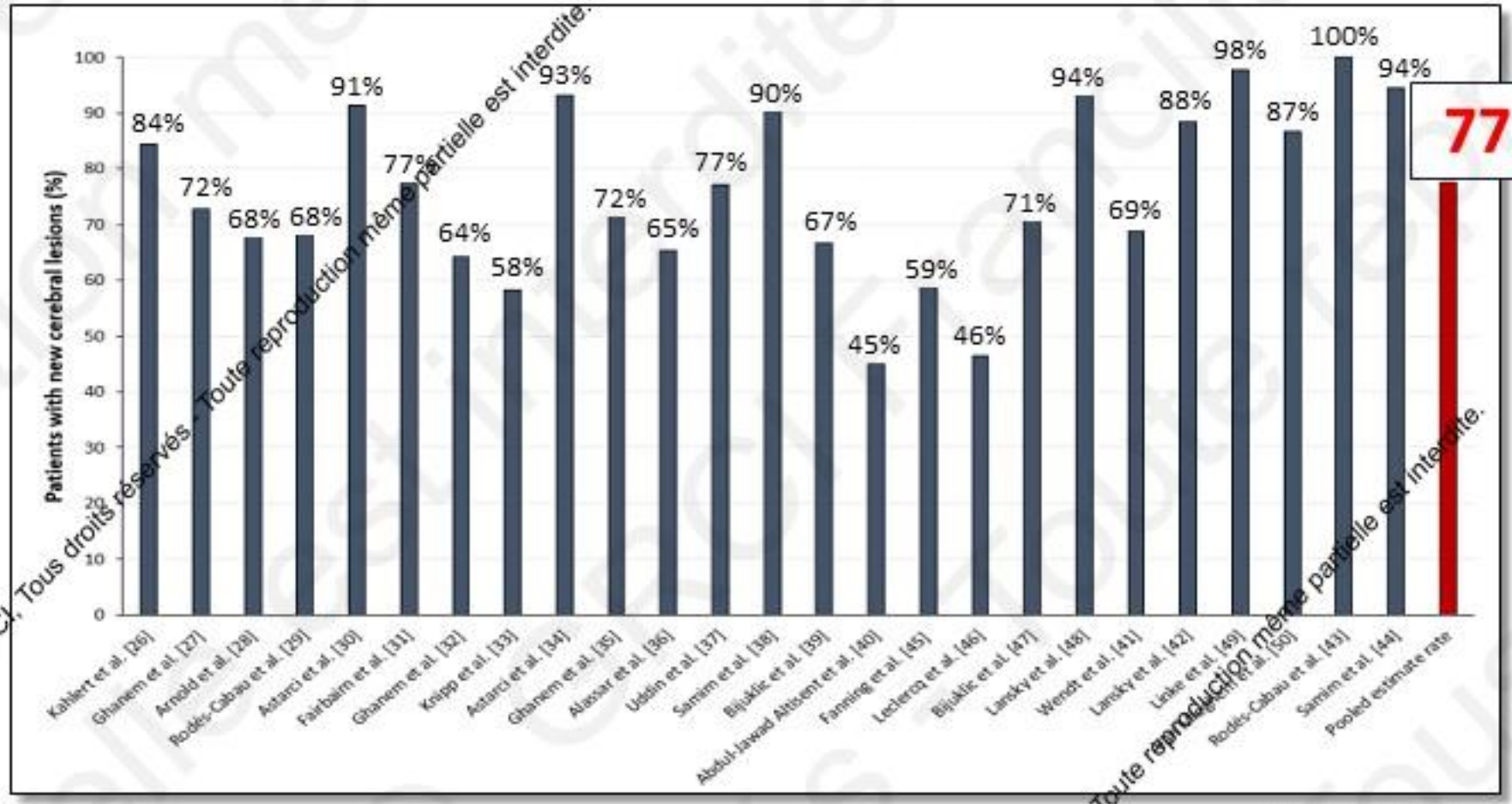
AVC, le sommet de l'iceberg



Hassell, M. E. C. et al. Nat. Rev. Cardiol. 2013; 10, 696–706

IRM post-TAVI

% of patient with new cerebral ischemic lesions on DW-MRI



Pagnesis et al. Int J Cardiol 2016

Nouvelles lésions cérébrales (DW-MRI)

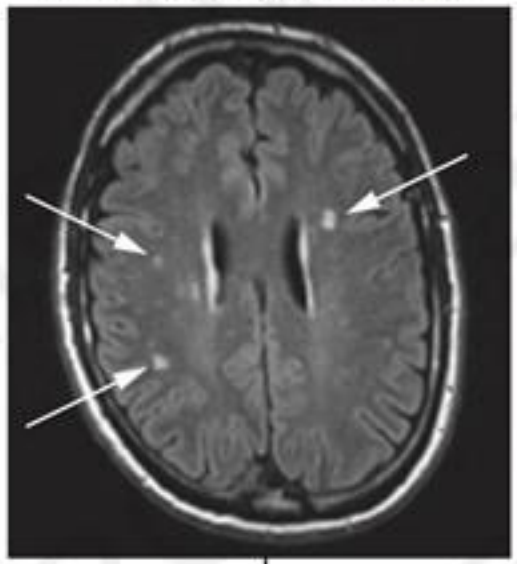
Fréquentes dans toutes les procédures de cardiologie interventionnelle

Table 1 Estimated Annual U.S. Patients With New Brain Lesions

Procedures	No. of Annual U.S. Patients	Incidence of New Brain Lesions, %	No. of Annual U.S. Patients With New Brain Lesions
Coronary angiography	1,072,000	11–17	118,000–182,000
Percutaneous coronary intervention	596,000	11–17	66,000–101,000
Coronary artery bypass graft	242,000	16–51	39,000–123,000
Surgical aortic valve replacement	90,000	38–47	34,000–42,000
Atrial fibrillation ablation	72,000	8–18	6,000–13,000
Transaortic valve implantation	10,000	68–91	7,000–9,000
Carotid endarterectomy	93,000	4–34	4,000–32,000
Carotid artery stenting	70,000	15–67	11,000–47,000
Cerebral angiography	300,000	11–20	33,000–60,000
Endovascular aneurysm	30,000	10–64	3,000–19,000
Total	2,600,000	13–24	321,000–628,000

Gress D, J Am Coll Cardiol. 2012; 23;60(17):1614-6

Impact clinique des infarctus cérébraux silencieux



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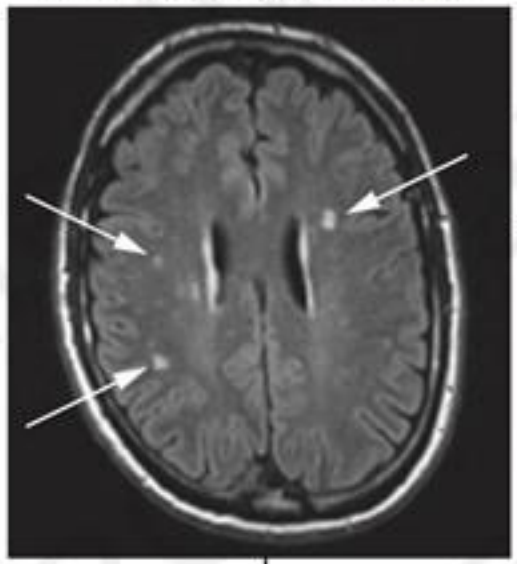
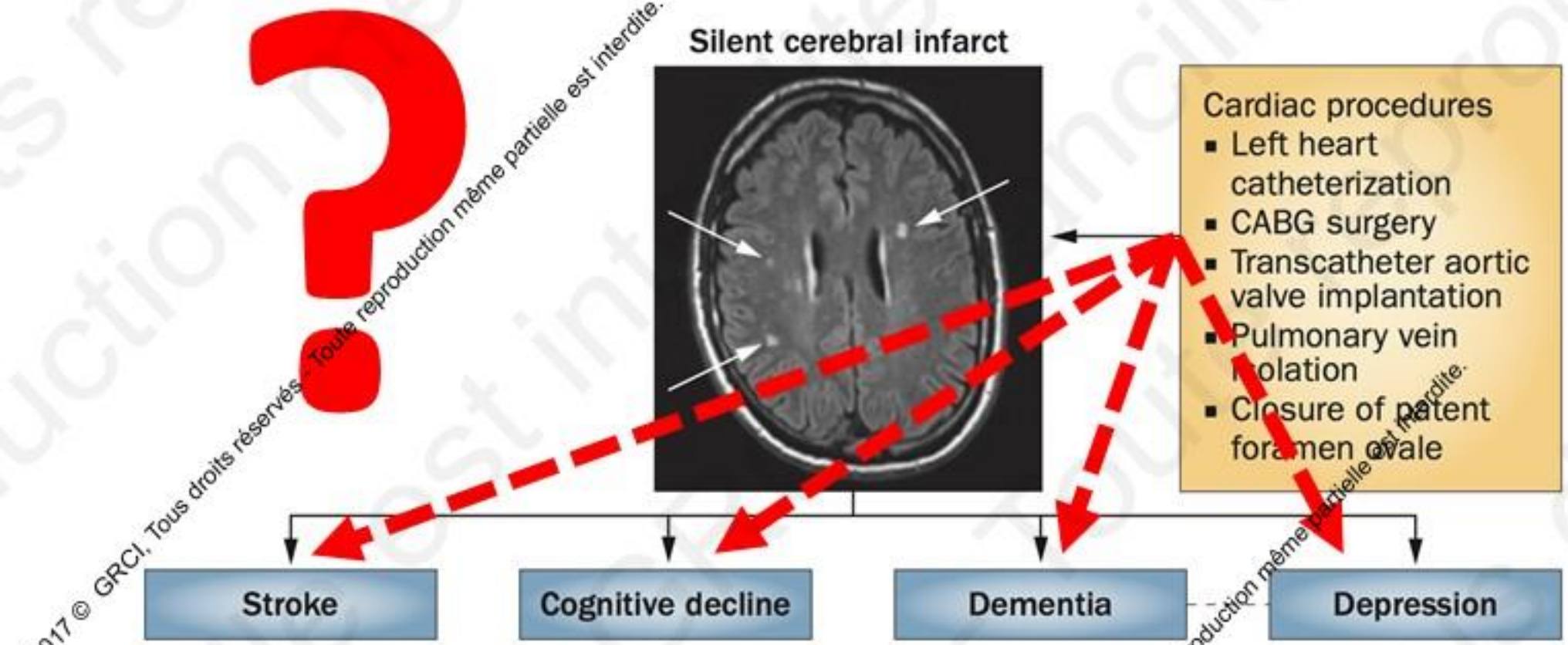


Cardiac procedures
- Left heart catheterization
- CABG surgery
- Transcatheter aortic valve implantation
- Pulmonary vein isolation
- Closure of patent foramen ovale

Stroke | **Cognitive decline** | **Dementia** | **Depression**

Hassell, M. E. C. et al. Nat. Rev. Cardiol. 2013; 10, 696–706

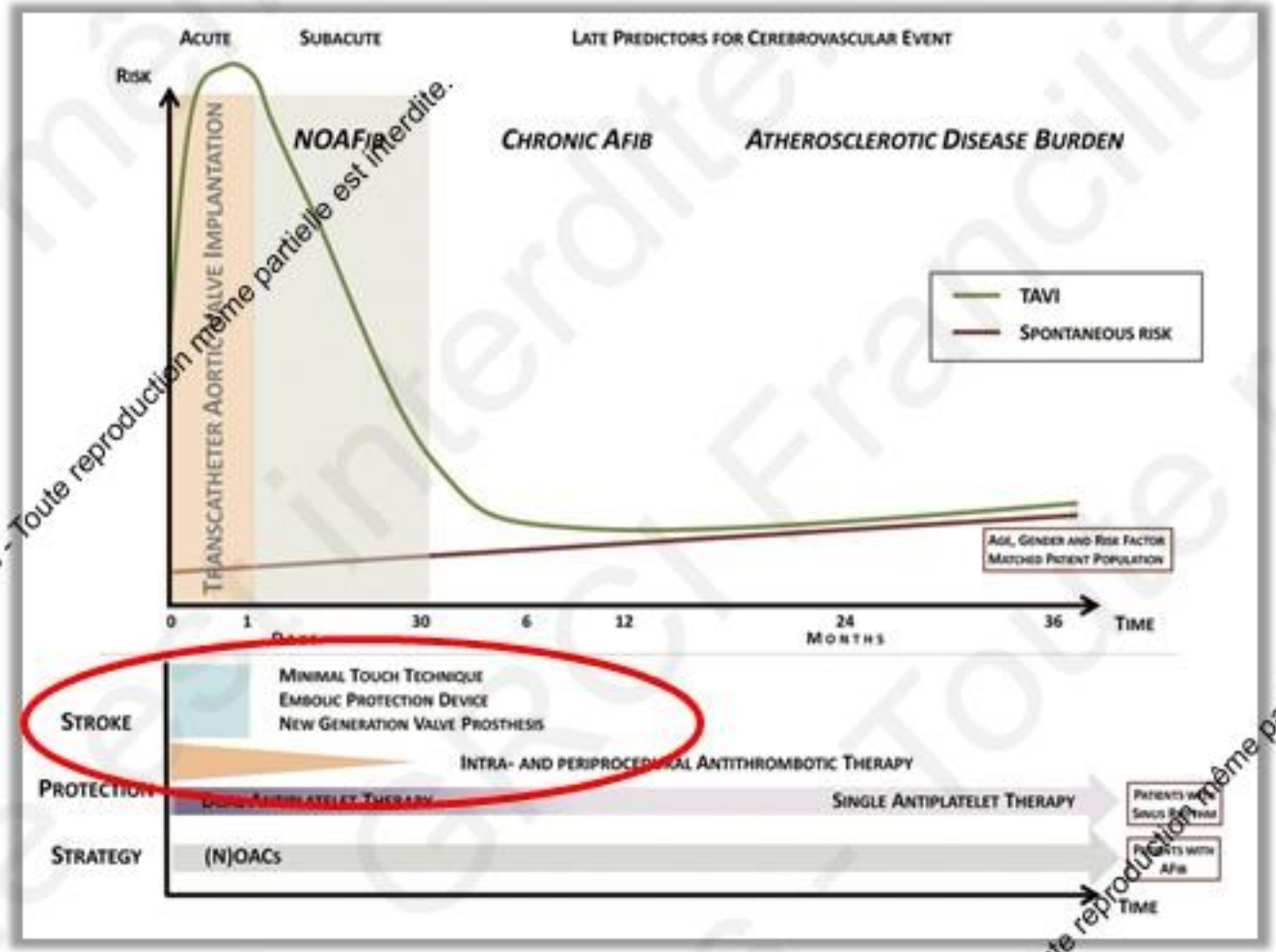
Impact clinique des infarctus cérébraux silencieux



Hassell, M. E. C. et al. Nat. Rev. Cardiol. 2013; 10, 696–706

Comment les diminuer ?

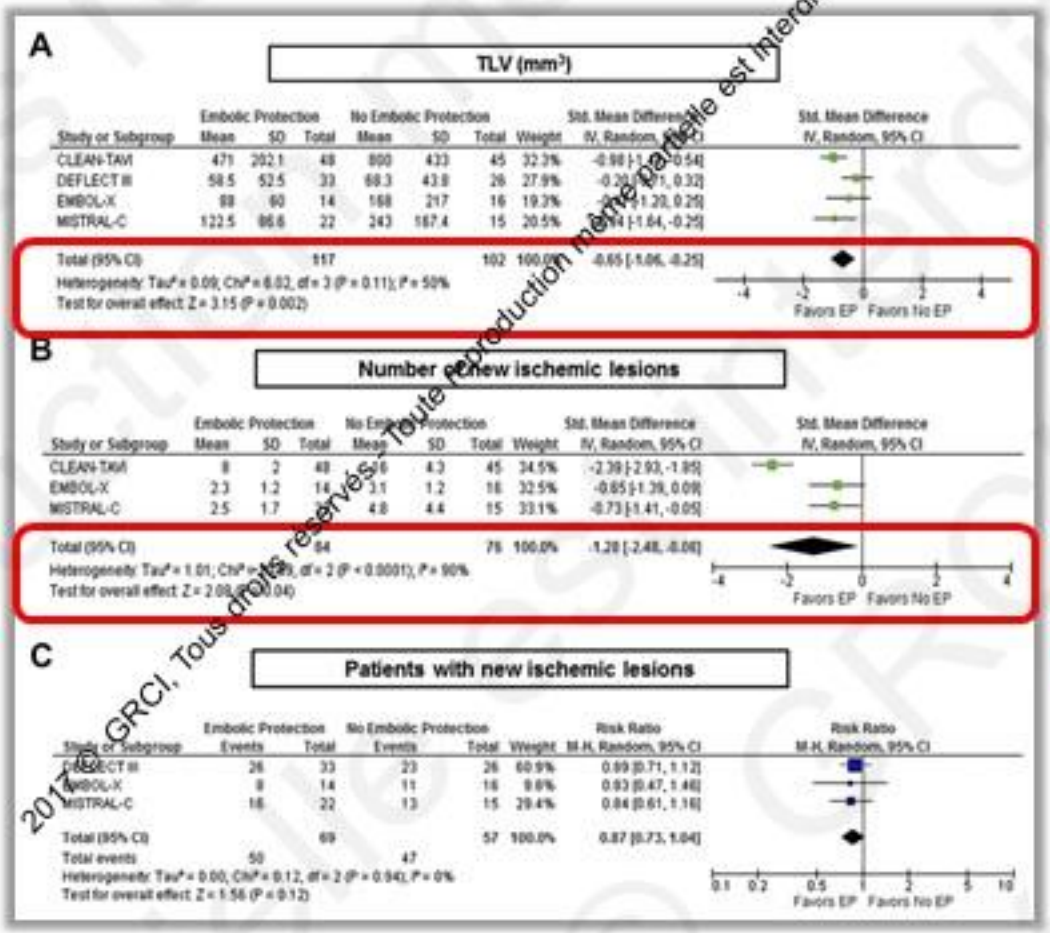
Prévention des AVC: risque procédural vs risque spontané



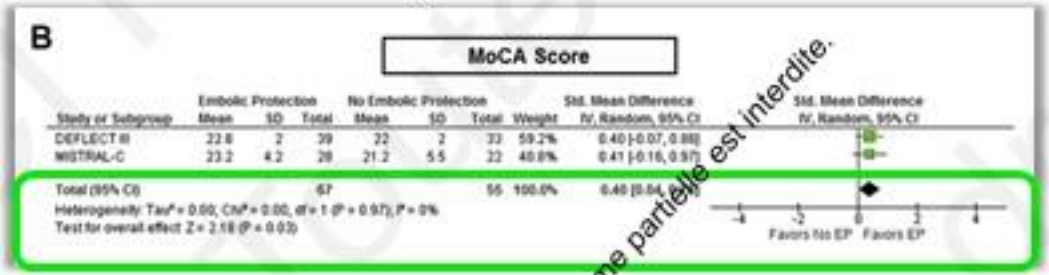
Stortecky, Circulation. 2012;126:2921-2924

Les systèmes de neuroprotection

Meta-Analysis of Randomized Controlled Trials



Montreal cognitive assessment score

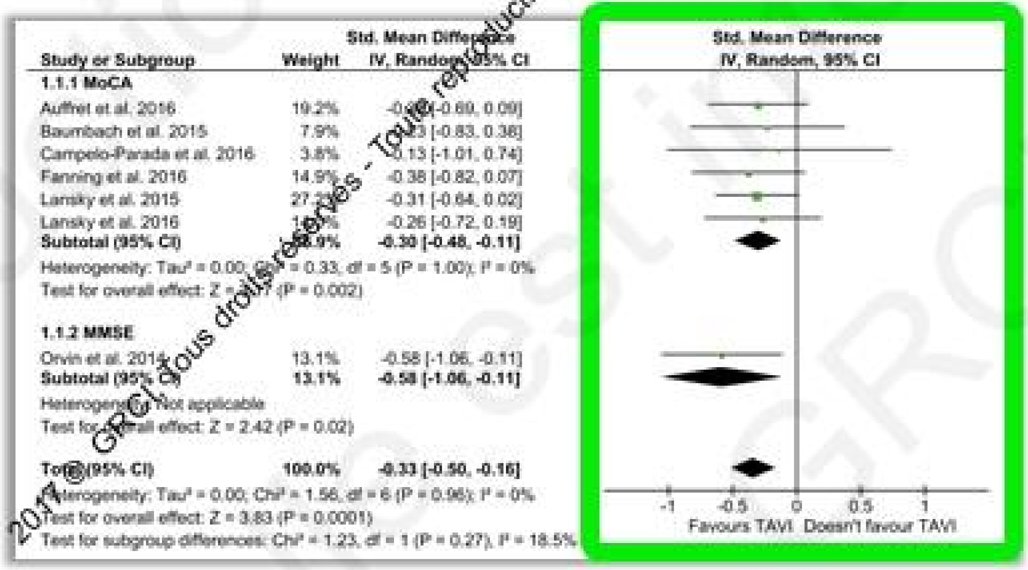


Giustino et al. J Am Coll Cardiol Intv 2016

Déclin cognitif post-TAVI ?

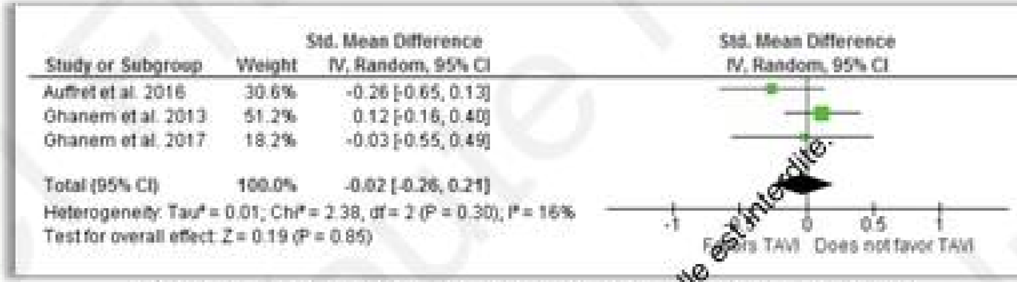
Méta-analysis: 18 études, n=1065, age moyen ≥80

1 month-cognition after TAVI



(change in cognitive score before and 1 month post-TAVI)

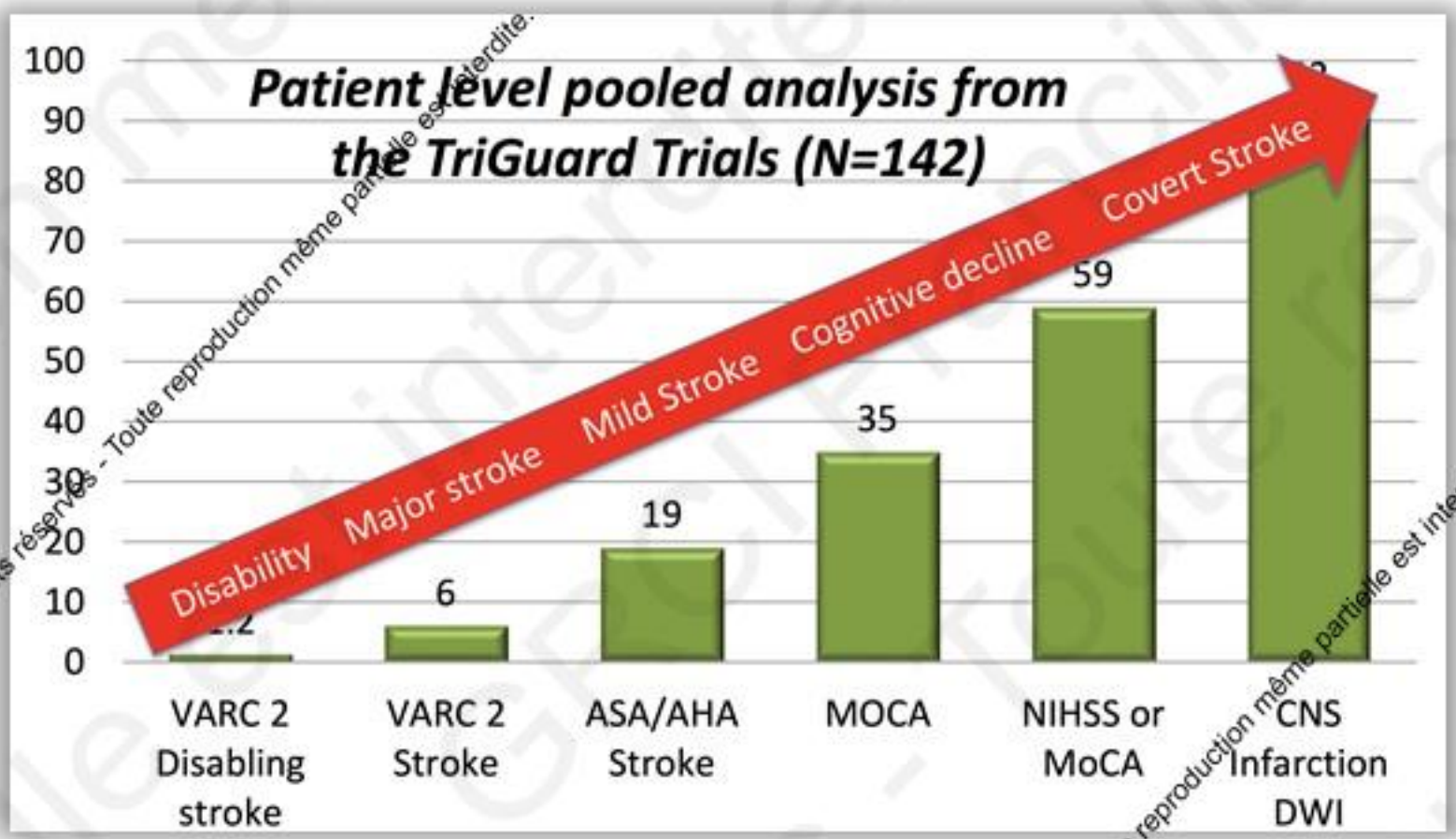
Long-term cognition (12-34 months following TAVI)



(change in cognitive score before and after TAVI in long-term)

Khan M, J Am Geriatr Soc 2017

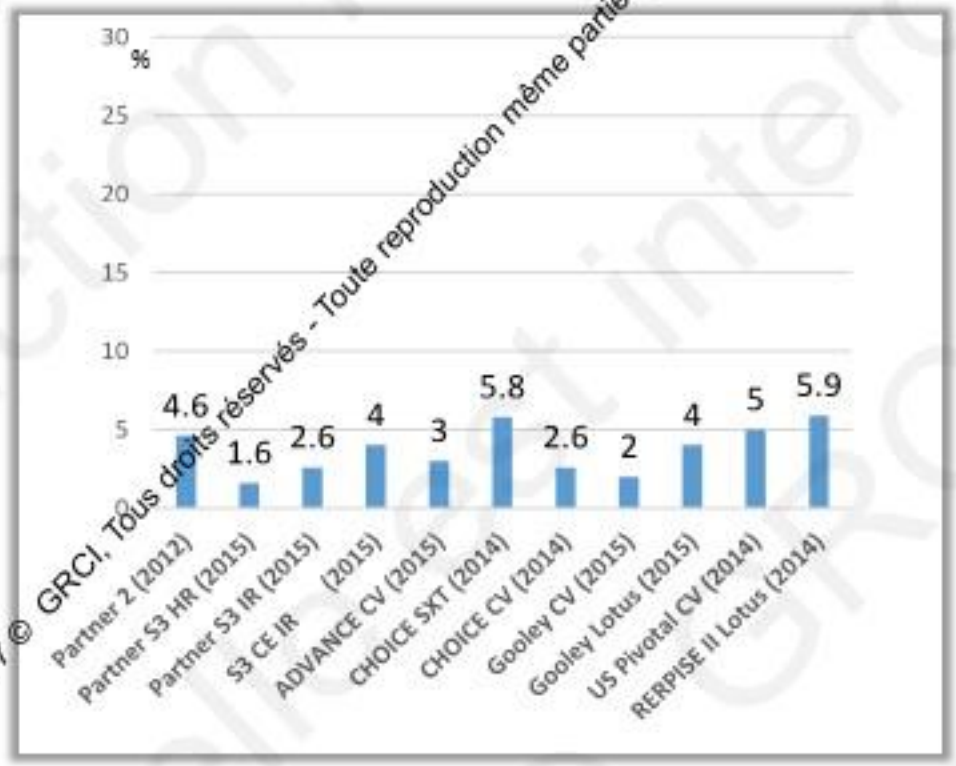
Qu'est ce qu'une complication neurologique?



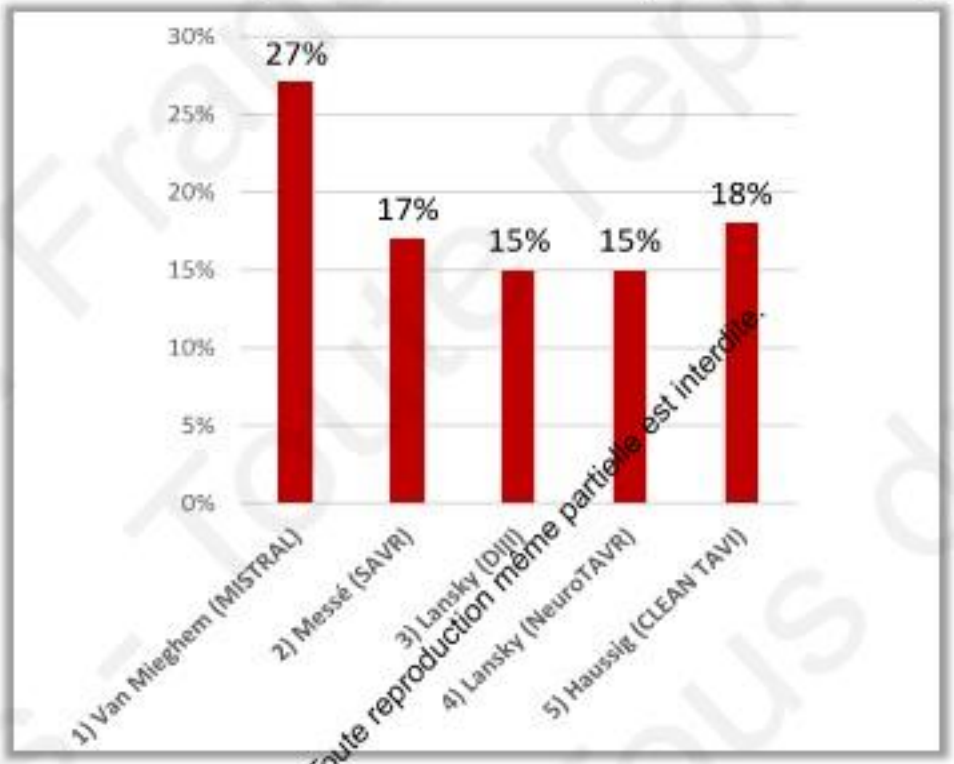
Lansky, Euro-PCR 2016

AVC sous-rapportés dans les études TAVI

Reported disabling stroke rates range from 1.6%-5.9% in TAVR trials



Stroke rates is 15-27% after TAVR by current AHA/ASA definitions (tissue-based)



Lansky, Euro-PCR 2016

Neuro ARC Recommendations

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

THE PRESENT AND FUTURE

REVIEW TOPIC OF THE WEEK

Proposed Standardized Neurological Endpoints for Cardiovascular Clinical Trials

An Academic Research Consortium Initiative

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European Heart Journal (2017) 00, 1–11
doi:10.1093/eurheartj/ehx037

CURRENT OPINION

Proposed Standardized Neurological Endpoints for Cardiovascular Clinical Trials

An Academic Research Consortium Initiative

Alexandra J. Lansky[1,2,3], Steven R. Messé[4], Adam M. Brickman[5], Michael Dwyer[6], H. Bart van der Worp[7], Ronald M. Lazar[5], Cody G. Pietras[1,2], Kevin J. Abrams[8], Eugene McFadden[9], Nils H. Petersen[10], Jeffrey Browndyke[11], Bernard Prendergast[12], Vivian G. Ng[1,2], Donald E. Cutlip[13], Samir Kapadia[14], Mitchell W. Krucoff[15], Axel Linke[16], Claudia Scala Moy[17], Joachim Schofer[18], Gerrit-Anne van Es[19], Renu Virmani[20], Jeffrey Popma[21], Michael K. Parides[21], Susheel Kodali[22], Michel Bilello[23], Robert Zivadinov[6], Joseph Akar[1], Karen L. Furie[24], Daryl Gress[25], Szilard Voros[26], Jeffrey Moses[22], David Greer[10], John K. Forrest[1], David Holmes[27], Arie P. Kappetein[28], Michael Mack[29], Andreas Baumbach[2]

Framework on how to assess, measure and classify neurologic endpoints associated with cardiovascular procedures

International Multi Stakeholder Consensus

NeuroARC

Definitions and Classification Relevant to Patients, Comprehensive, Practical

Lansky A, Messe S, Baumbach A et al.; JACC 2017 and EHJ 2017

Type 1: Overt CNS Injury (Acutely Symptomatic)		
Type 1a	**Ischemic Stroke**	Focal or multi-focal vascular territory Symptoms ≥24 hours or until death or Symptoms <24 hours with neuroimaging confirmation
Subtype 1aH: Ischemic Stroke with Hemorrhagic conversion		**Class A**: Petechial Hemorrhage **Class B**: Confluent Hemorrhage (with space occupying effect)
Type 1.b	**Intracerebral Hemorrhage**	Symptoms (focal or global) caused by an intraparenchymal or intraventricular bleed
Type 1.c	**Subarachnoid Hemorrhage**	Symptoms (focal or global) caused by a subarachnoid bleed
Type 1.d	**Stroke, not otherwise specified**	Symptoms ≥24 hours or until death, without imaging
Type 1.e	**Hypoxic-Ischemic Injury**	Global neurologic symptoms due to diffuse brain injury attributable to hypotension and/or hypoxia
Type 2: Covert CNS Injury (Acutely Asymptomatic brain injury detected by NeuroImaging)		
Type 2.a	**Covert CNS Infarction**	Acutely asymptomatic focal or multi-focal ischemia, based on neuroimaging
Subtype 2aH: Ischemic Stroke with Hemorrhagic conversion		**Class A**: Petechial Hemorrhage **Class B**: Confluent Hemorrhage (with space occupying effect)
Type 2.b	**Covert Cerebral Hemorrhage**	Neuroimaging or Acutely asymptomatic CNS hemorrhage on neuroimaging that is not caused by trauma
Type 3: Neurologic Dysfunction without CNS Injury (Acutely Symptomatic)		
Type 3.a	**Transient Ischemic Attack (TIA)**	Symptoms <24 hours with no evidence of acute infarction by neuroimaging
Type 3.b	**Delirium without CNS injury**	Transient non-focal (global) neurologic signs or symptoms (variable duration) without evidence of cell death by pathology or neuroimaging

Neuro ARC s'applique à tous les essais CV

Les endpoints neurologiques doivent être adaptés à la procédure et au device étudiés.

TABLE 2 Recommended Endpoints and Assessments by Device or Procedure Category

	Category I: Neurological Injury as Procedural and Long-Term Safety Measure	Category II: Neurological Injury as Procedural Efficacy Measure	Category III: Neurological Injury as Procedural Safety and Long-Term Efficacy Measure
Device/procedure type	Devices or procedures with inherent iatrogenic embolic risk, for example: • Surgical cardiac or ascending aorta procedures (valve replacement, CABG, ascending aorta, and aortic arch replacement) • Transcatheter cardiac procedures (TAVR, MVR, LV devices for heart failure) • Thoracic endovascular aortic repair	Devices or procedures designed to prevent iatrogenic or spontaneous acute neurological injury, for example: • Neuroprotection devices • Cerebral temperature management devices	Devices or procedures with inherent iatrogenic embolic risk and designed for prevention of spontaneous long-term risk, for example: • Atrial fibrillation ablation • PFO or LAA closure • Carotid interventions • Adjunctive pharmacotherapy trials
Suggested endpoints	Early and long-term safety endpoints • Overt CNS injury (Type 1) • CNS infarction and CNS hemorrhage • Neurological dysfunction (Type 3) • Cognitive change (overall) Optional early safety endpoints • MRI total lesion volume • Covert CNS injury (Type 2)	Early efficacy endpoints • Overt and covert CNS injury (Type 1 and 2) • CNS infarction and CNS hemorrhage • Neurological dysfunction (Type 3) • MRI total lesion volume • Cognitive change (overall and domain-specific)	Early safety and long-term efficacy endpoints • Overt CNS injury (Type 1) • CNS infarction and CNS hemorrhage • Neurological dysfunction (Type 3) • Cognitive change (overall and domain-specific) Optional early safety endpoints • MRI total lesion volume • Covert CNS injury (Type 2)

Lansky, JACC 2017 and EHJ 2017

Conclusion

- Existence d'un risque neurologique pour toutes procédures de cardiologie interventionnelle

- Large spectre du risque neurologique allant de l'AVC grave qui est rare, aux lésions ischémiques cérébrales asymptomatiques, fréquentes, mais dont le pronostic à long terme est discuté

- TAVI: une des procédures exposant le plus à ces complications, à l'origine de l'émergence des systèmes de neuroprotection

- Neuro ARC : Standardisation des « endpoints » neurologiques pour les futurs essais cliniques de cardiologie interventionnelle.