Cerebral Protection during Percutaneous Structural Cardiac Interventions

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Stroke Council, Prague 2016

ESC Working Group on Valvular Heart Disease

Valvular Heart Disease
ESC Working Group

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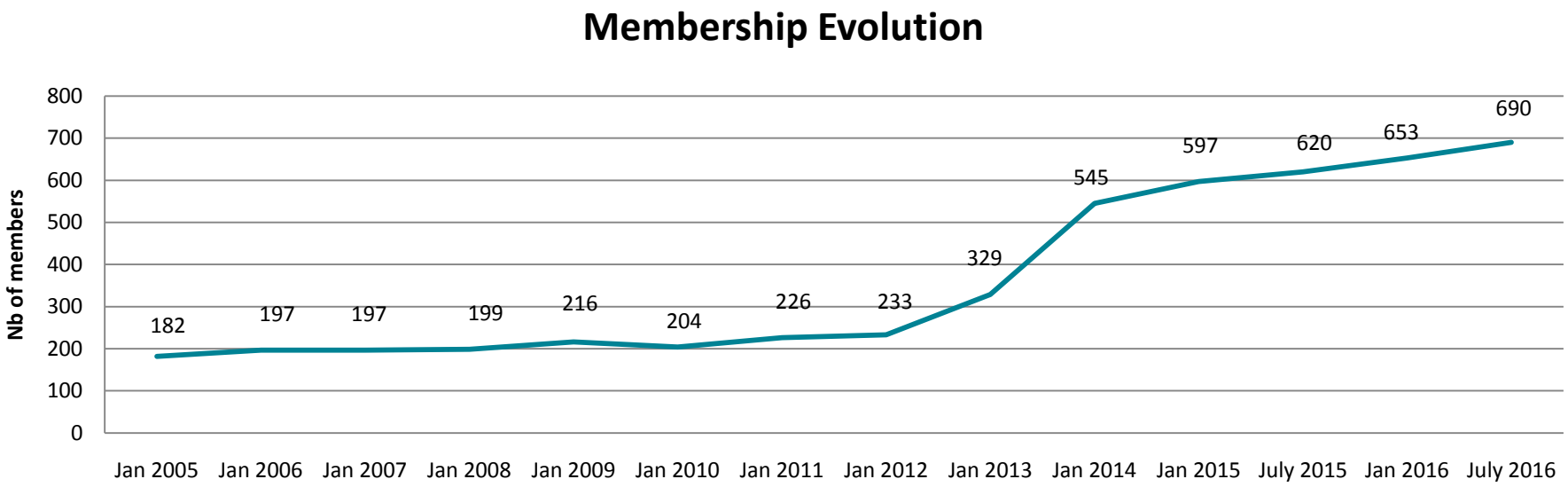
Membership: Evolution since 2005



Valvular Heart Disease
ESC Working Group

EUROPEAN SOCIETY OF CARDIOLOGY®

2015-2016 Achievements : Congresses & Meetings

Endorsed meeting:

EUROVALVE 2016

CONGRESS ENDORSED BY THE ESC WORKING GROUP ON VALVULAR HEART DISEASE

THURSDAY 10 - FRIDAY 11 MARCH 2016 (2DAYS), BRUSSELS -BELGIUM

Topic(s): *Valvular Heart Diseases;*

IN-PERSON EVENT

Summary

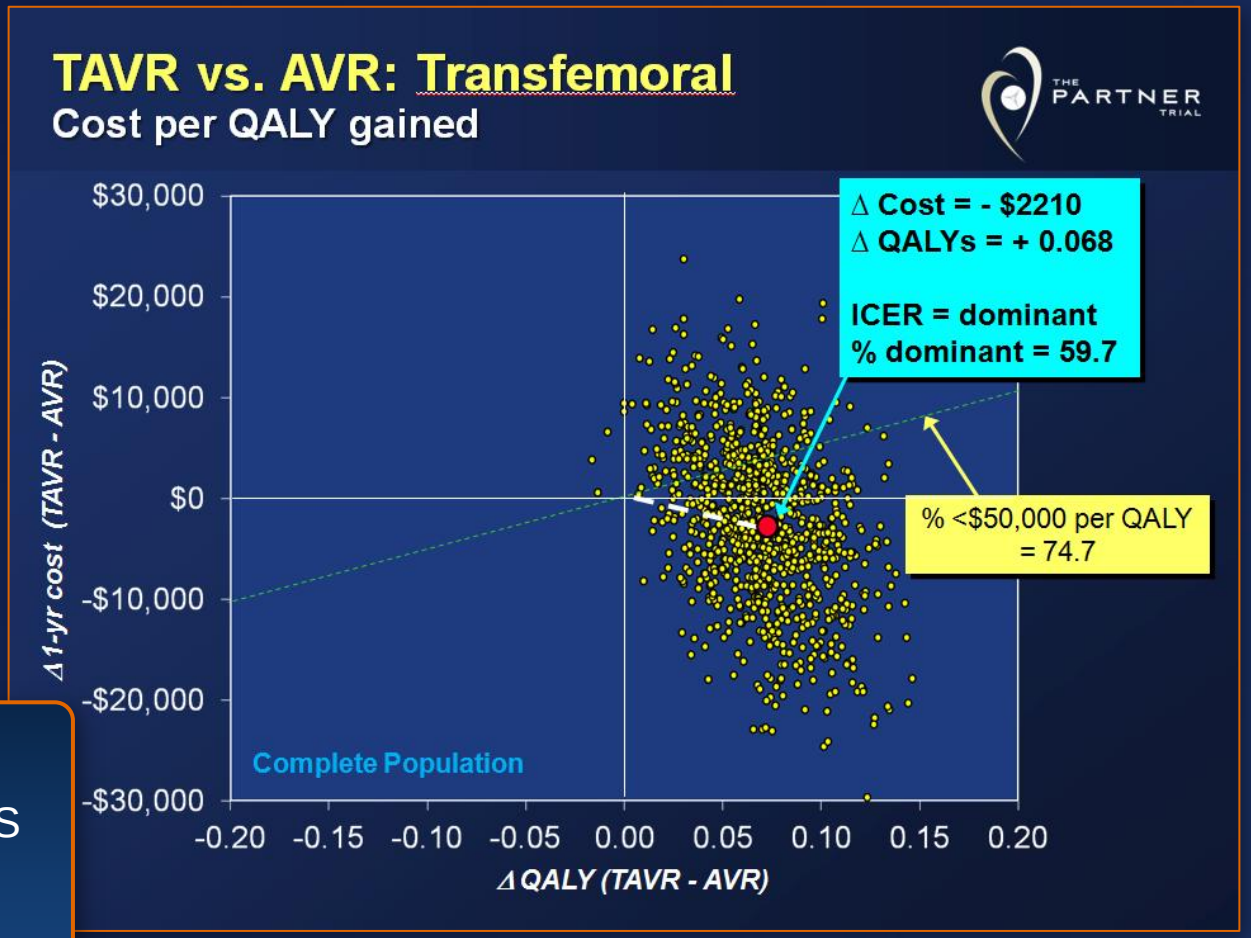
As part of the scientific committee and program, the Working Group on Valvular Heart Disease is happy to announce the endorsment of the fourth edition of the EuroValve Congress.

Aiming to promote optimal management of patients with valve disease, the congress addresses imagers, clinical cardiologists, interventionists and cardiac surgeons.

For this 2016 edition, it will take place at the hotel Bloom in Brussels, Belgium, on 10-11 March and will feature several symposia, controversies and round tables with expert's panel.

Transfemoral TAVR is a Dominant Technology Over Surgery

- **Cost effective technology even with first generation devices**
- **Achieving better outcomes while reducing costs**



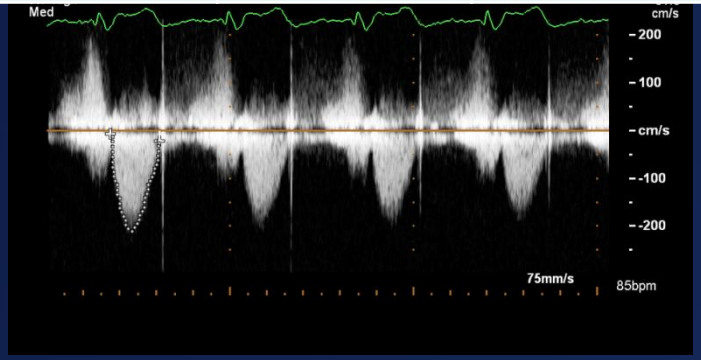
Key Insights

- TF-TAVR reduced LOS by 6 days vs. AVR
- TF-TAVR resulted in improved early QOL

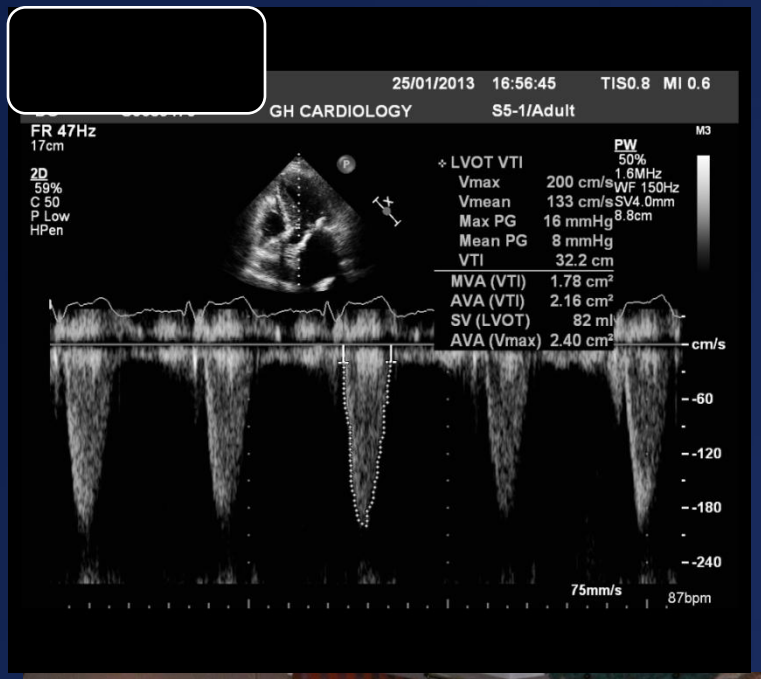
Reynolds M., Cost Effectiveness of Transcatheter Aortic Valve Replacement Compared With Surgical Aortic Valve Replacement in Patients With Severe Aortic Stenosis: Results from The PARTNER Trial (Cohort A). Presented at TCT 2011, November 7, 2011; San Fransisco, California.

1st UK TAVI

	Peak Gradient (mmHg)	Mean gradient (mmHg)
Pre - TAVI	96	54
01/2007	11	5.5
2009	11	6
2011	17	9
2012	19	9
2013	16	8
2014	16	8
2015	18	9



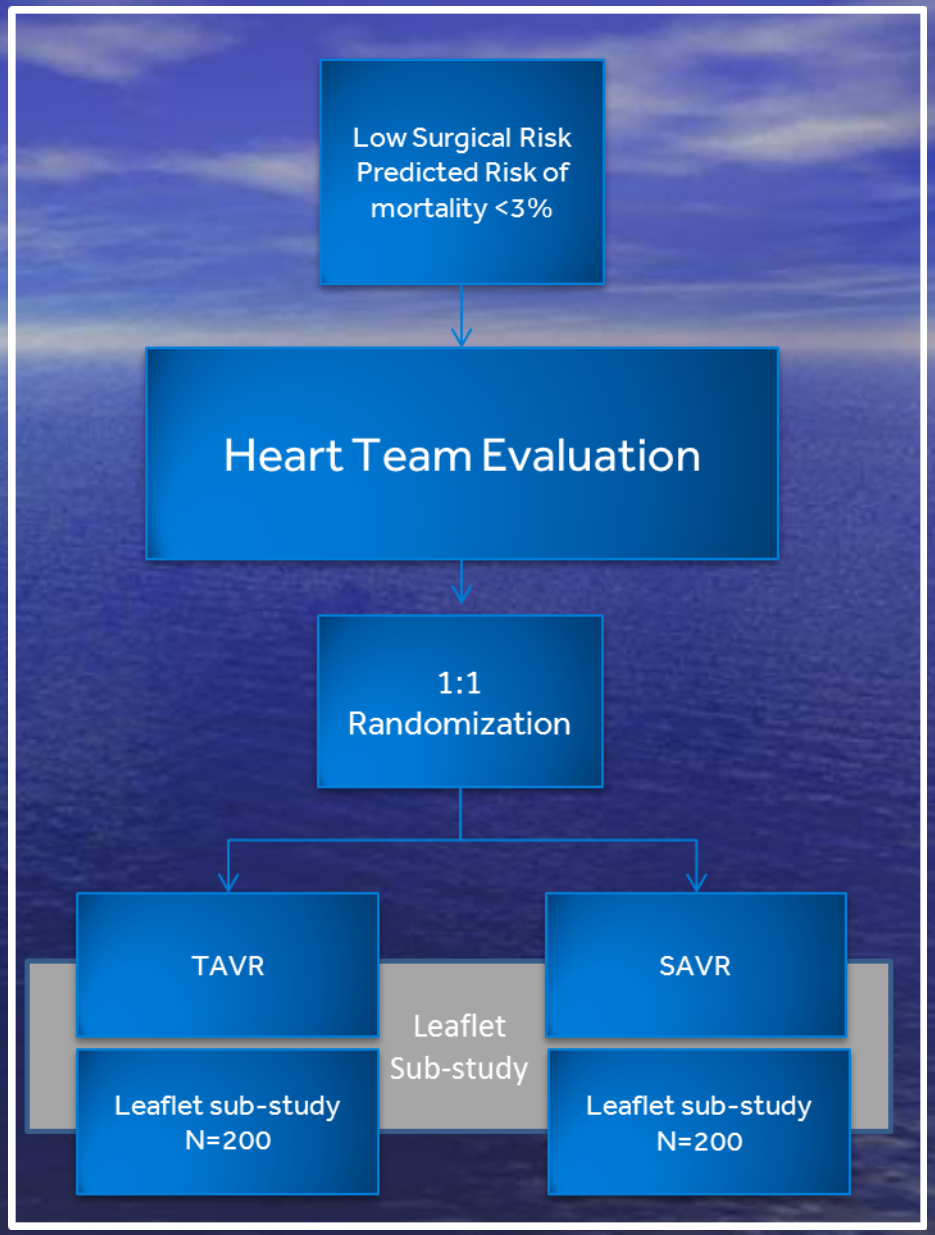
9th year post implant....



Moving to Loq Risk Patients

LOW RISK & LEAFLET SUB-STUDY

- **Patient Population: Low Risk Cohort**
  - Determined by Heart Team to be low surgical risk
- **Primary Endpoint:**
  - Safety: Death, all stroke, life-threatening bleeding, major vascular complications, or AKI at 30 days
  - Efficacy: Death or major stroke at 2 years
- **Sample Size: ~1200 Subjects**
- **Follow-up Evaluations:**
  - 30-days, 6-month , and 1 Through 5 years
- **Number of Sites: Up to 80 sites**

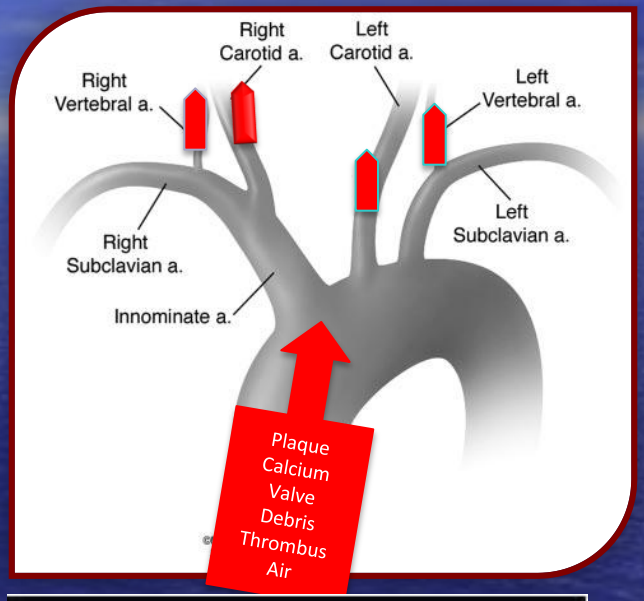


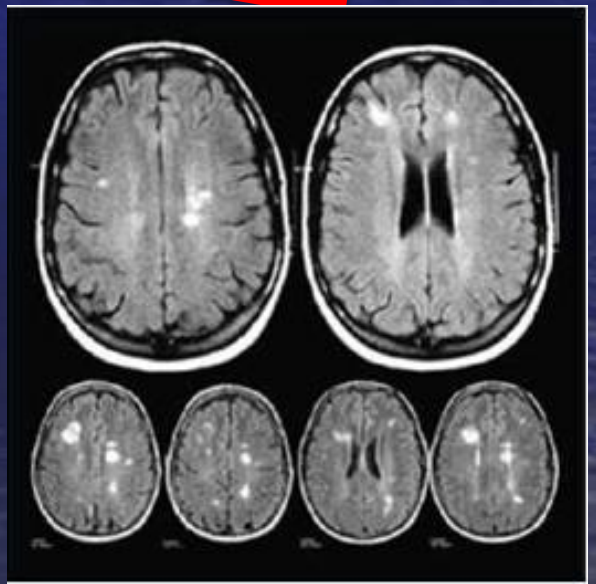
CLINICAL QUESTIONS

1. Is (embolic) stroke during TAVI/R a relevant clinical problem ?
2. Is there clinical/functional correlation of 'silent' microembolic events ?
3. Can we improve outcomes with embolic protection devices ?

Background

- Stroke is a rare but devastating complication of TAVI
- 50% of events occur periprocedurally
- Clinically 'silent' or non-detected strokes are frequent
- New embolic lesions in the brain can be detected in up to 100% of patients following a TAVI procedure
- Embolic events have been linked to neurocognitive decline

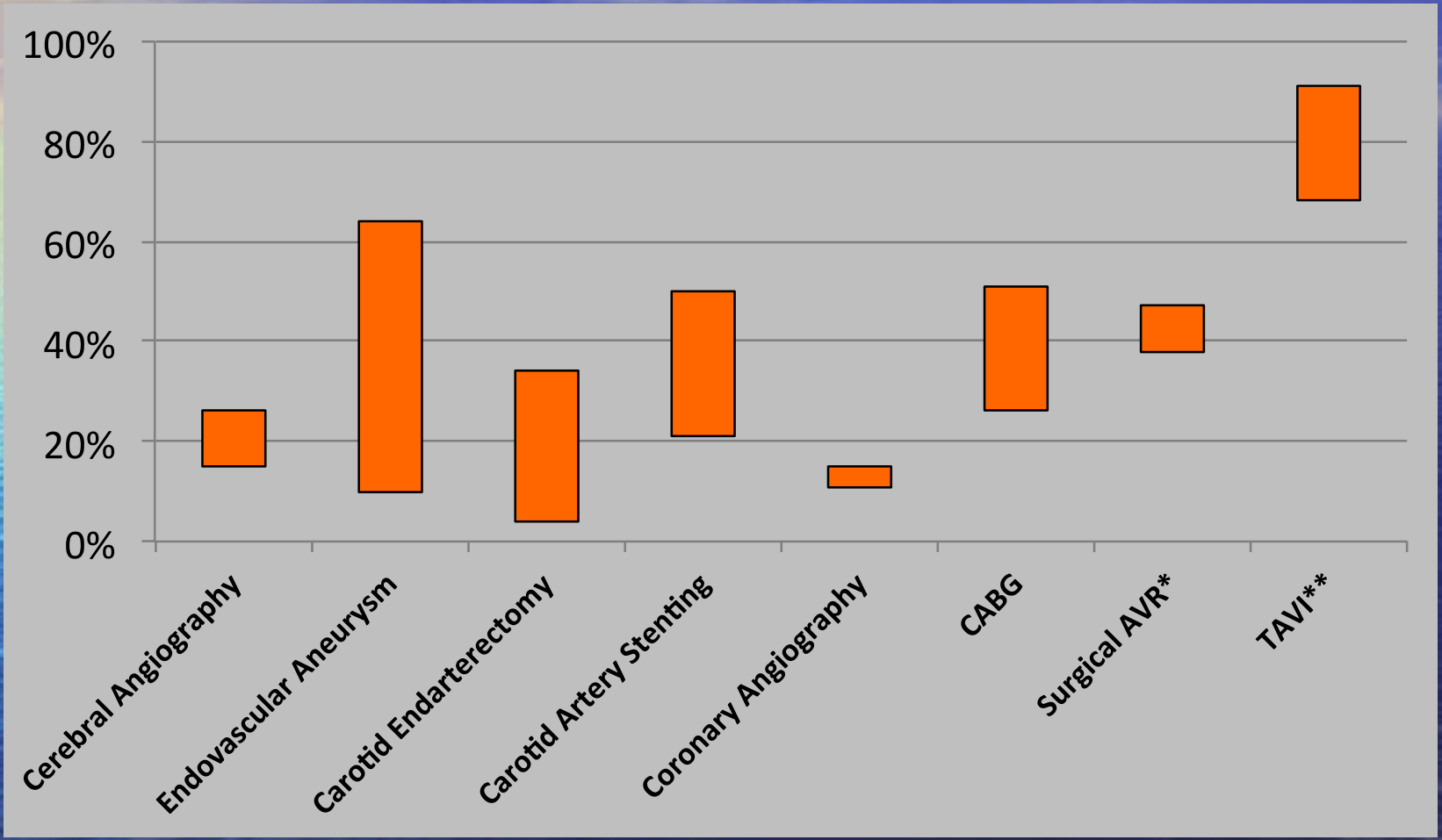




Postoperative cognitive capacity

cognitive decline
memory
mood disturbances
psychomotor speed
personality changes

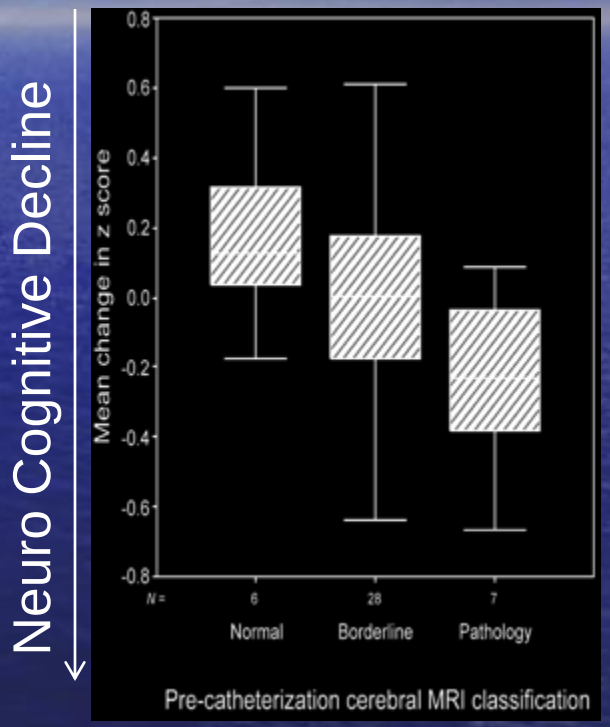
Incidence of New Brain Lesions



*Knipp 2005, Stolz 2004.
**Astarci 2011, Ghanem 2010, Kahlert 2010, Rodés-Cabau 2011.

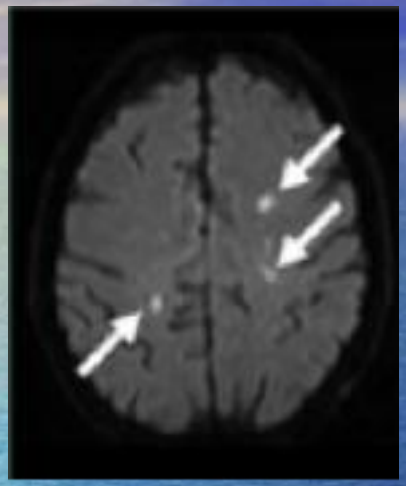
Neurocognitive Decline
and New Lesions

- Pre-existing and new lesions on DW-MRI after catheterization is related to cognitive decline
- Patients with new ischemic lesions post CABG (20%) had a larger neurocognitive decline than the patients with stable
- The link between new lesions on DW MRI in TAVI cohort yet to be established..



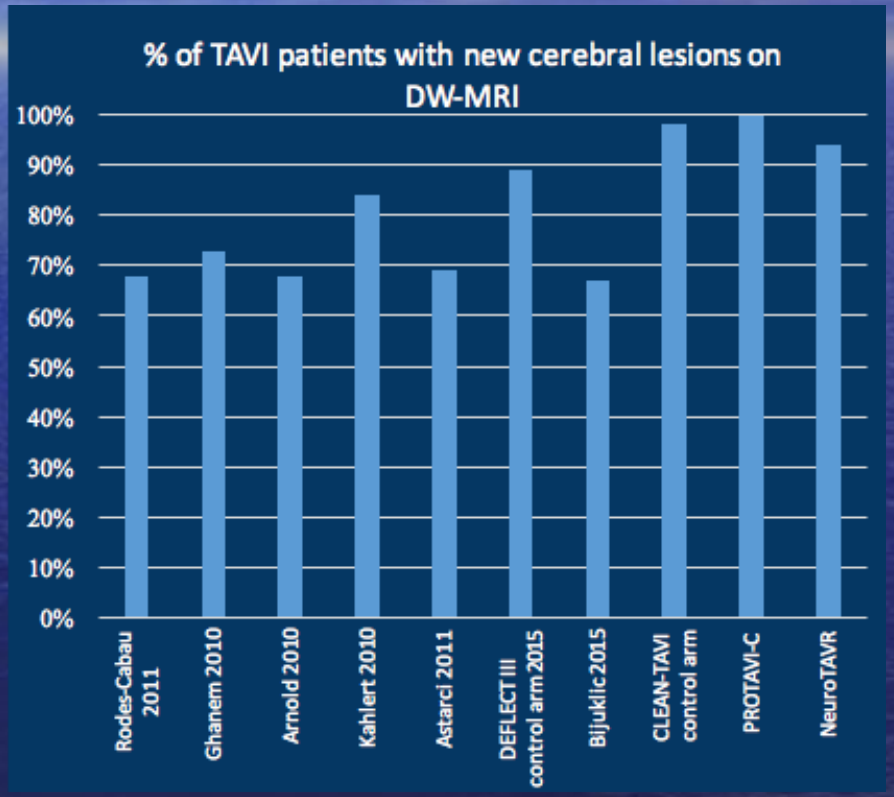
Lund et al, 2005 Restrepo et al Stroke 2002

MRI imaging is "truly frightening" post TAVI…



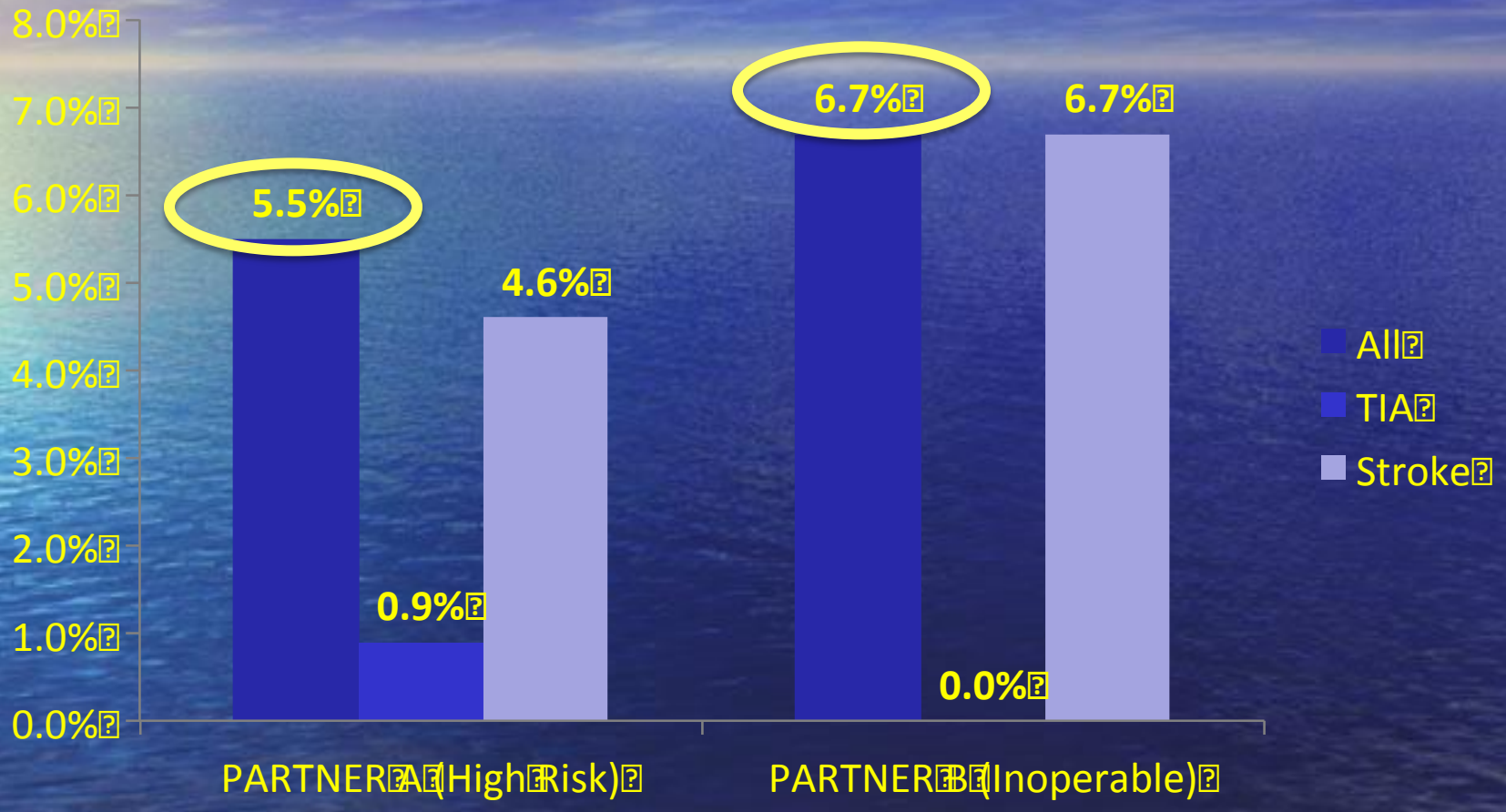
Ghanem, et. al, JACC 2010

- 68-100% of TAVI patients affected[1-10]
- Most patients have multiple infarcts
- "Silent" infarcts associated with[11-13]
  - 2-4-fold risk of future stroke
  - >3-fold risk of mortality
  - >2-fold risk of dementia
  - Cognitive decline
  - Dementia



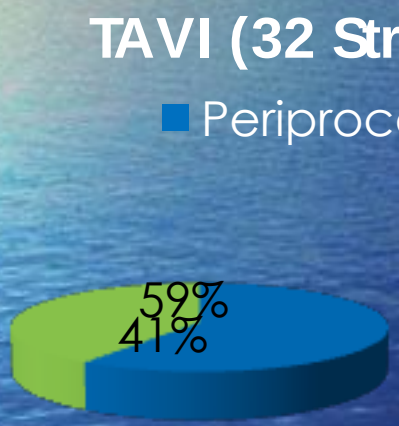
Insight from Pivotal studies

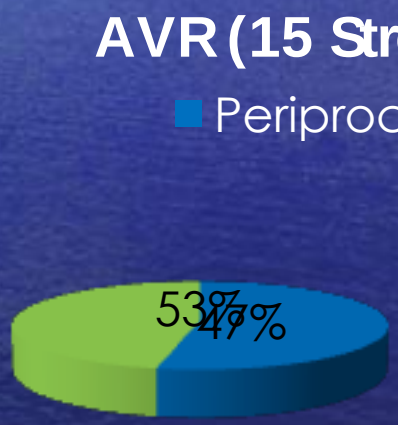
Acute Manifestations: PARTNER A and B (30-Day Events)



Smith et al. N Engl J Med 2011;364:2187-98. Leon et al. N Engl J Med 2010;363:1597-1607.

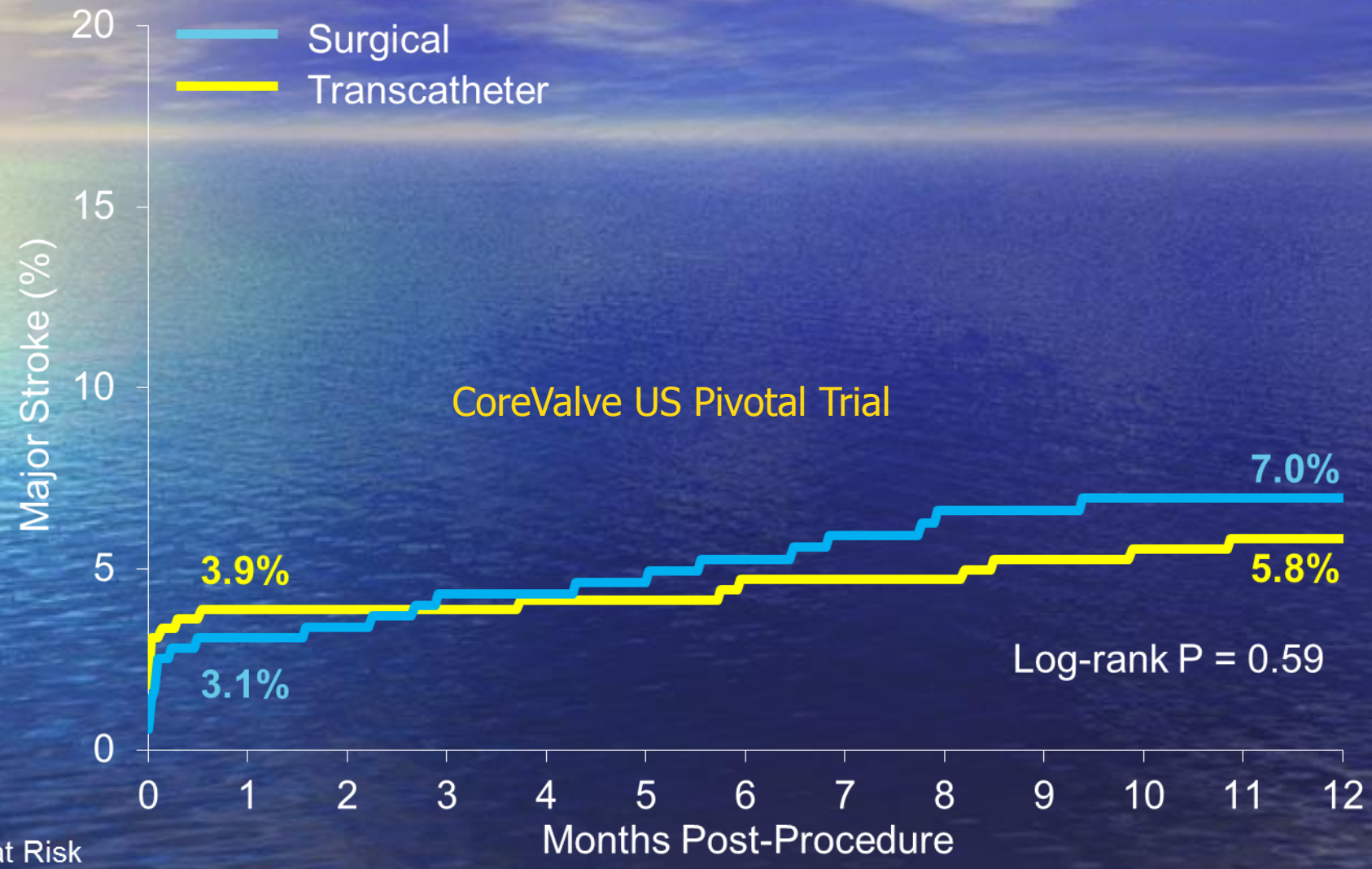
Timing of Neurological Events
PARTNER (Cohort A)





Major Stroke

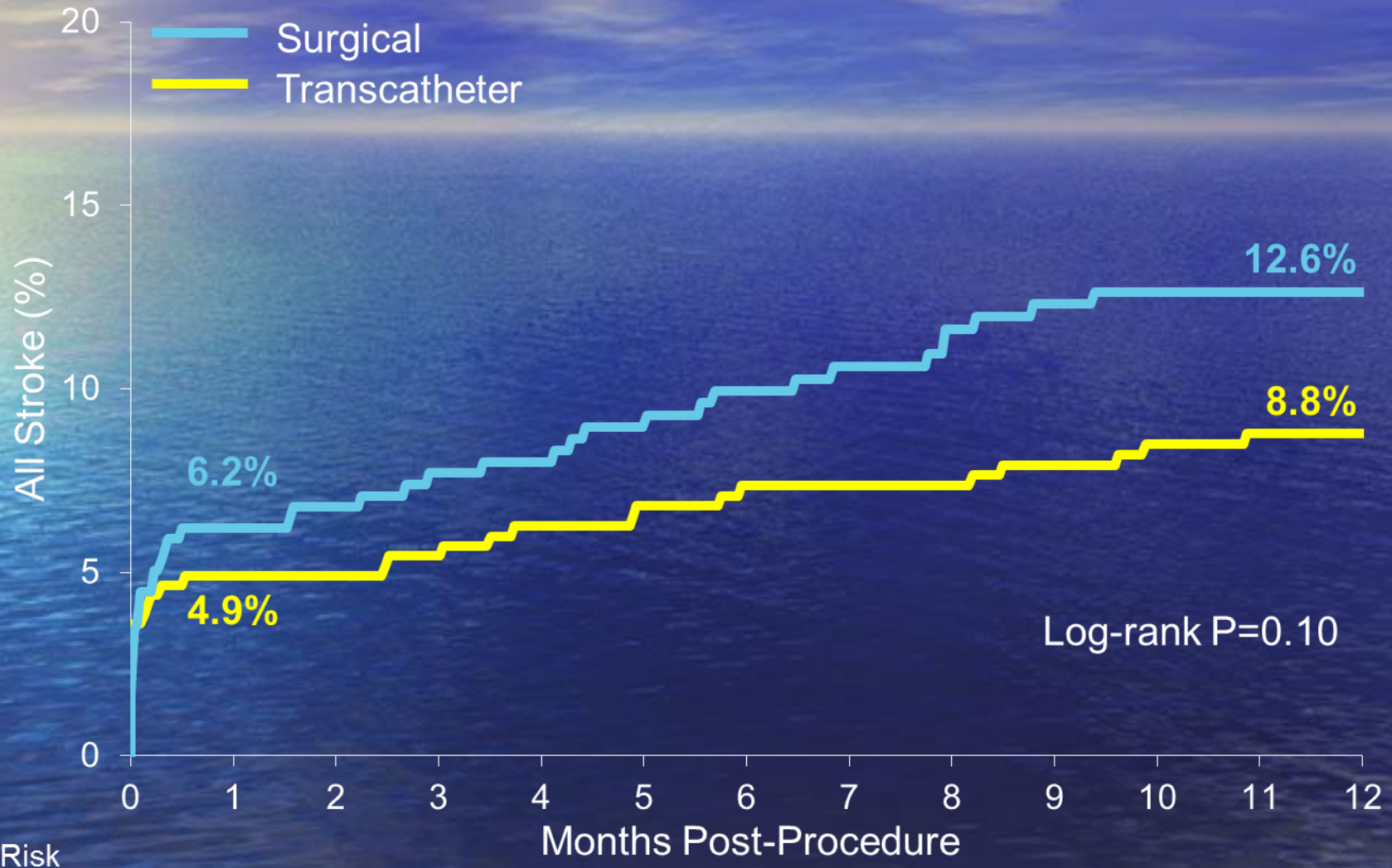
CoreValve US Pivotal Trial



No. at Risk					
Surgical	357	333	289		263
Transcatheter	390	367	344		322

All Stroke

CoreValve US Pivotal Trial



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

National registry-FRANCE 2

- N 3191 pts undergoing TAVI
- 3.98% reported CVE
  - 55% major strokes
  - 14.5% minor strokes
  - 30.5 % TIA
- Predictors: advanced age, multiple valves

Tchetche et al. J Am Coll Cardiol Intv 2014;7: epub

FRANCE 2: Timing of CVE

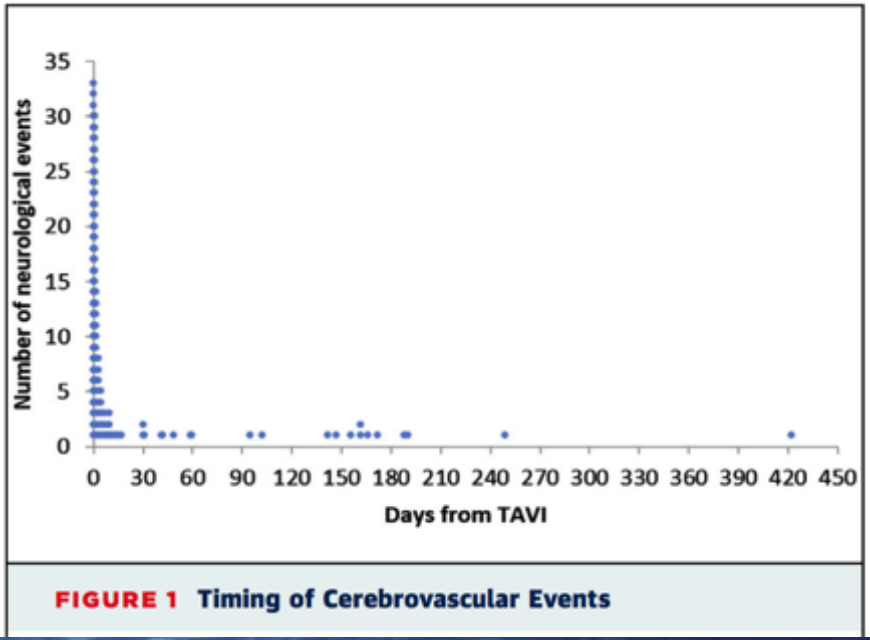


FIGURE 1 Timing of Cerebrovascular Events

50% periprocedural
Majority of major strokes on day 1

Time From Date of Valve Placement (in Calendar Days)	No.	Mean	SD	Median	Range
Overall	131	22.9	59.5	2	0–422
Major stroke	72	21.3	52.8	1	0–249
Minor stroke	19	28.2	96.3	2	0–422
Transient ischemic attack	40	23.1	48.8	2	0–188

Tchetche et al. J Am Coll Cardiol Intv 2014;7: epub

Mechanisms of peri-procedural stroke

Embolic

- Wire and catheter manipulation
- BAV
- Device positioning in the root
- Valve deployment
- Post-dilatation

Haemorrhagic

- Bolus dose heparin
- Severe hypertension

Global Ischaemia

- Severe hypotension
- Rapid pacing

And while Procedural Mortality Improves with Experience

Improved One Year All Cause Mortality following Transcatheter Aortic Valve Implantation (TAVI) Beyond The Learning Curve Experience: Insights From Glenfield-Leicester UK TAVI Registry.

Ashan Gunarathne[1], Elved Roberts[1], Derek Chin[1], Dave Adlam[1,2], Alison Beech[1], Mariuca Vasa-Nicotera[2], Amerjeet Banning[1,2], Rebecca Horton[1], Hasan Jilaihawi[3], Jan Kovac[1,2]

[1]Glenfield Hospital, University Hospital Leicester NHS Trust, Leicester, United Kingdom, [2]University of Leicester, United Kingdom, [3]University

Introduction

Transcatheter aortic valve implantation (TAVI) is rapidly evolving as a therapeutic option for patients who are at high risk for conventional surgical AVR with favourable mortality benefit. The successful outcomes of this procedure are partly driven by the operator skills, expertise & experience. The impact of "learning curve experience" on one year all-cause mortality post TAVI implantation by a single operator in a single centre has not been previously investigated.

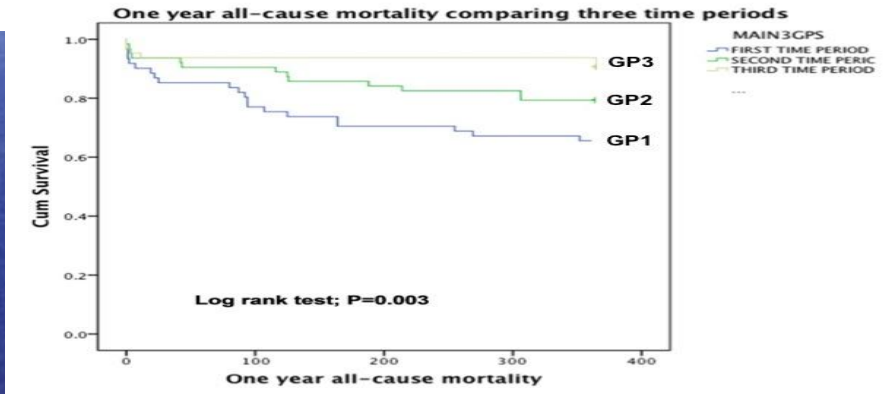
Objective: To analyze & to observe any secular trends in one year all cause mortality in consecutive patients who received TAVI in a tertiary cardiac centre in the UK over a five year period to observe the impact of "learning curve experience" on mortality rates.

Methods

The registry records of 188 consecutive TAVI patients (2007-2013) were reviewed using patient-level data. One year all-cause mortality data was obtained from the national mortality data base and collated with local registry demographic, risk profile and TAVI procedure related information. Kaplan-Meier analysis was used to compare mortality between the "first 60 patients" (learning curve experience group, GP1) to other age, gender & risk profile matched two equal sequential groups (GP2 & GP3).

Results

Of the total population (n=188, mean age: 82(SD:6) yrs) 50% were male. Use of trans femoral access (93.6%) was significantly ($P<0.05$) higher compared to the trans-apical route. Corevalve was the most commonly used implant (68.4%). The majority of the patients had a higher logistic Euroscore (median: 16.6(IQR :10-22)). Smoking (54.4%) & diabetes (20.2%) were the most commonly prevalent risk factors. 17.8% of the patients required a PPM where 9% had at least one major complication (tamponade, CVA, Major



In univariate mortality analysis, event free survival was significantly higher (91.6% vs. 65.46%) in the latter time periods [GP 2 & 3: n=128] compared to the "learning curve experience-group"[GP1: n=60], (log rank rest, P=0.003) (graph 1). Procedure related characteristics (post TAVI aortic regurgitation, complications) were comparable between the groups, except the use of Corevalve(CV) was more prevalent in the first time period (CV: 91.7% vs. Edwards sapien (ES) :8.3%) compared to GP3 period (CV:43.8% vs. ES: 48.4%). In multivariate cox regression analysis, this disparity appeared not be associated with any improved mortality.

Conclusions

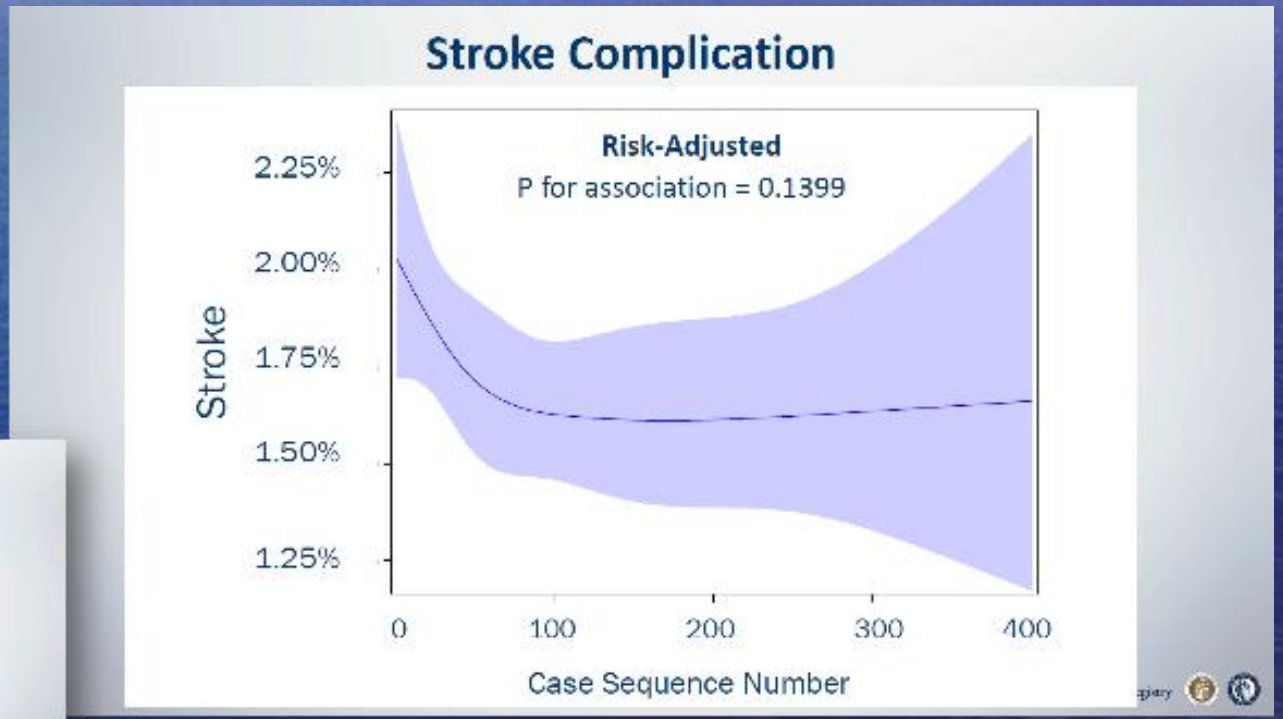
In our experience , One year all-cause mortality has improved and hospital stay has reduced over three consecutive time periods. The mortality reduction does not relate to patient related characteristics and may have been driven by acquired skills and experience of the TAVI team and advances in valve design. This warrants further investigations.

Stroke risk seem to be independent of operator experience

>53000 TAVI patients from >350 US centres

No decline in rates with increasing experience

'Self-reported' rates almost certainly an underestimate



No difference between ballon and self-expandable valves

	Odds Ratio (95% Confidence Interval)
Multicenter experience	
Transfemoral approach, %	2.4 (1.9–3.0)
Transapical approach, %	1.8 (1.1–2.8)
Transfemoral versus transapical approach	1.14 (0.75–1.74)
Single-center experience	
Transfemoral approach, %	3.9 (3.2–4.8)
Transapical approach, %	3.2 (2.2–4.8)
Transfemoral versus transapical approach	1.06 (0.61–1.85)
Multicenter experience	
CoreValve, %	2.2 (1.6–3.1)
Edwards Valve, %	2.5 (1.8–3.4)
CoreValve versus Edwards Valve	1.10 (0.79–1.51)
Single-center experience	
CoreValve, %	4.1 (3.1–5.4)
Edwards Valve, %	3.0 (2.1–4.3)
CoreValve versus Edwards Valve	1.28 (0.43–3.81)

Athappan et al JACC 2014;63:2010-10

Other procedural factors

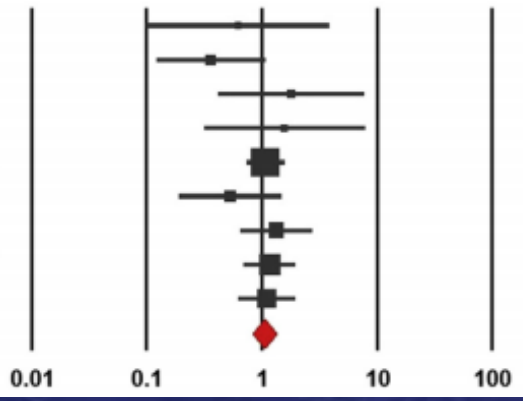
Predictors of acute (≤24 h) cerebrovascular events				
Balloon postdilation	2.51 (1.15–5.49)	0.017	2.46 (1.07–5.67)	0.034
Valve dislodgment/embolization	3.97 (1.32–11.94)	0.029	4.36 (1.21–15.69)	0.024
Aortic valve area (per 0.1-cm^2 decrease)	1.21 (0.97–1.53)	0.086	1.22 (0.96–1.53)	0.097
NYHA functional class III–IV	5.68 (0.77–42.01)	0.071	5.06 (0.68–37.77)	0.114

Predictors of subacute (1-d–30-d) cerebrovascular events				
New-onset atrial fibrillation	2.96 (1.21–7.25)	0.023	2.76 (1.11–6.83)	0.028
Severely calcified aorta	2.59 (1.13–5.97)	0.032	2.28 (0.98–5.30)	0.056
Diabetes mellitus	2.27 (1.02–5.03)	0.039	2.17 (0.97–4.84)	0.060

Nombela-Franco et al Circulation 2012;126:3041-53

Does access site play a role- perhaps not..?

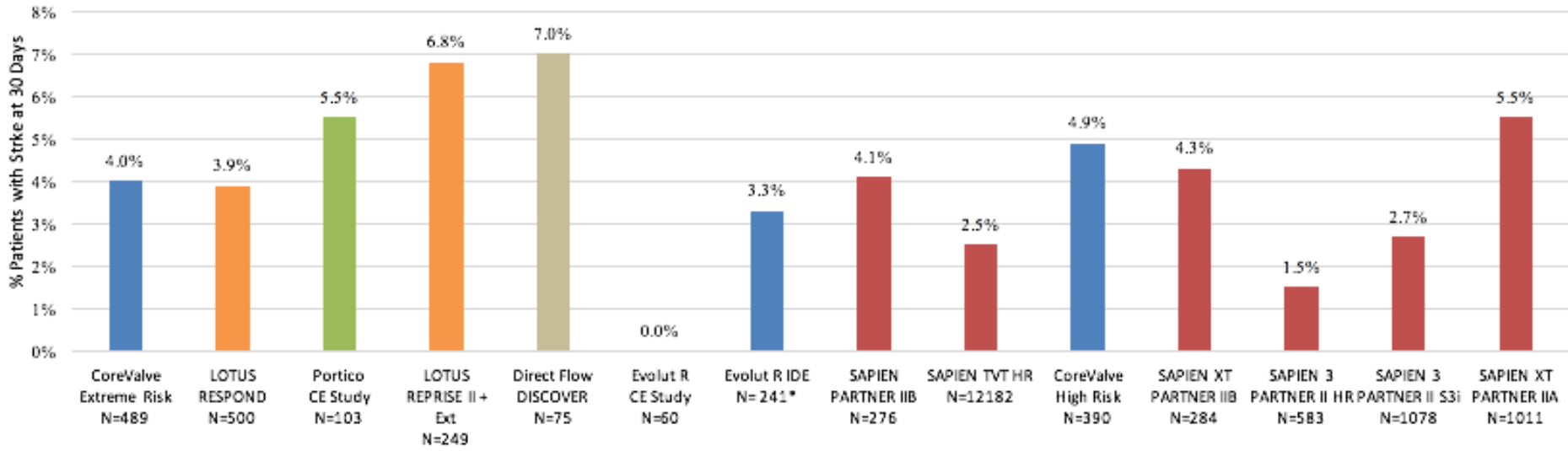
Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	Events / Total Group-A	Events / Total Group-B
ANZ Source	0.615	0.099	3.811	-0.522	0.602	2 / 67	3 / 63
Belgium	0.360	0.123	1.058	-1.858	0.063	7 / 232	7 / 88
Canada	1.779	0.418	7.564	0.780	0.435	5 / 168	3 / 177
France Registry	1.568	0.318	7.743	0.552	0.581	7 / 161	2 / 71
GARY	1.072	0.740	1.552	0.368	0.713	100 / 2694	41 / 1181
PARTNER I cohort A	0.531	0.192	1.465	-1.223	0.221	9 / 244	7 / 104
Sentinel EORP/TCV T	1.331	0.654	2.708	0.789	0.430	54 / 3390	9 / 749
SOURCE Registry	1.168	0.702	1.943	0.598	0.550	27 / 920	35 / 1387
SOURCE XT	1.100	0.632	1.915	0.337	0.736	39 / 1694	19 / 906
Overall	1.042	0.830	1.307	0.354	0.723		



Large meta analysis (29000 patients!) showed no effect of access site

Athappan et al JACC 2014;63:2010-10

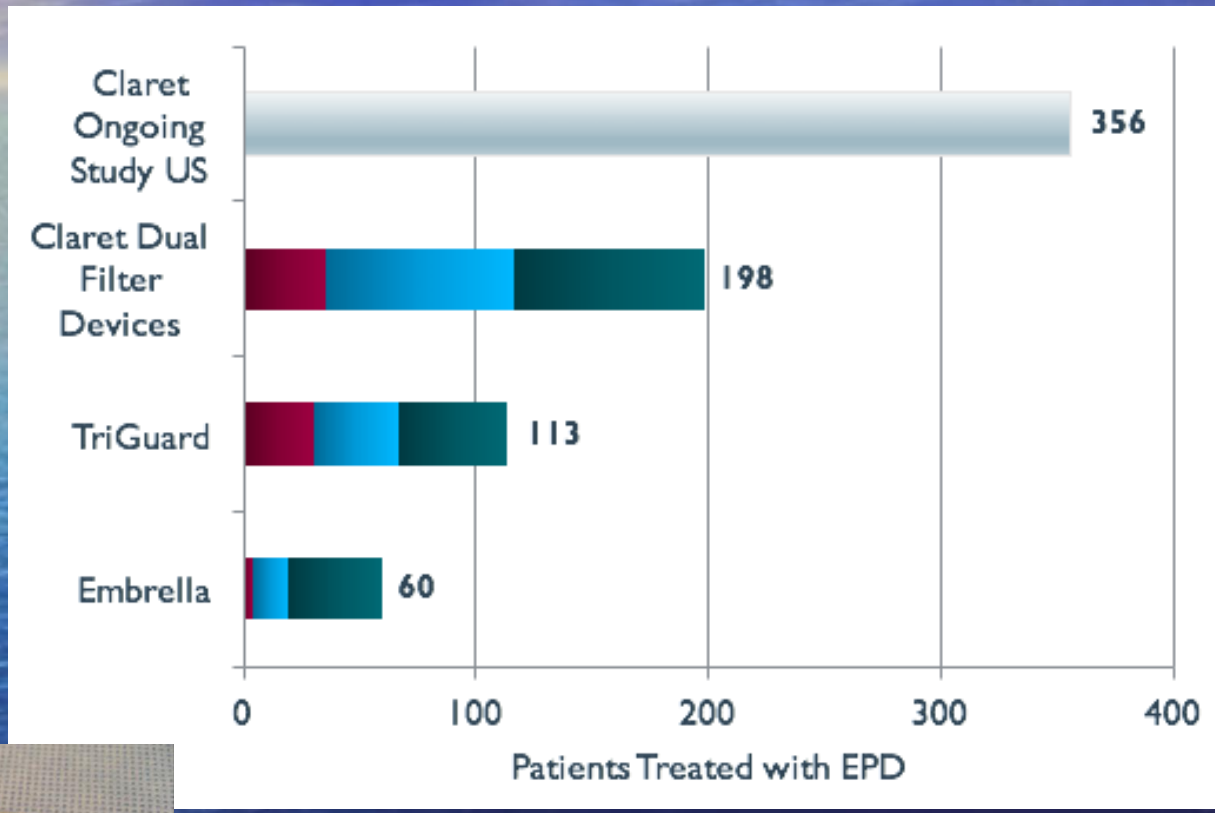
2nd generation devices and in intermediate risk patients-Stroke Remains Issue

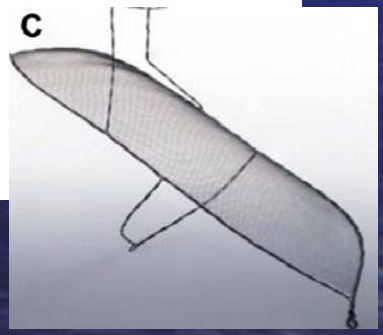


Meredith, et al., presented at PCR London Valves 2014; Adams, et al., *N Engl J Med* 2014; 370: 1790-8; Leon, et. al. presented at ACC 2013; Lefevre et al., *J Am Coll Cardiol* 2016; 1:; Popma, et al., *J Am Coll Cardiol* 2014; 63: 1972-81; Linke, et. al. presented at London Valves 2015; Van Mieghem, et al., presented at EuroPCR 2015; Kodali, et al., presented at ACC 2015; Holmes, et al., *JAMA* 2015; 313: 1019-28; Meredith, et al., presented at ACC 2015, ' Williams, et. al. presented at ACC 2016; Thourani, et al, presented at ACC 2016

Can we improve outcomes with embolic protection devices ?

Can we improve outcomes with embolic protection devices ?





Bonhoffer et al J Am Coll Cardiol 2002;39:1664-9

Claret data

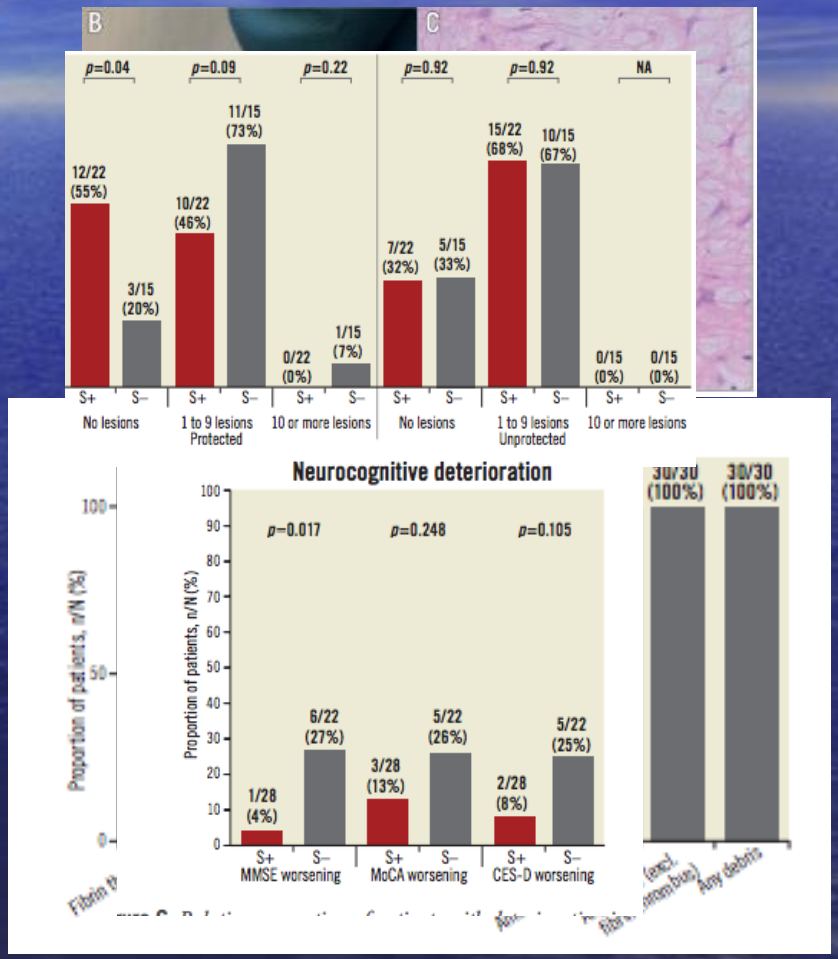
It does seem effective in capturing debris..

MISTRAL-I trial of 66 patients randomised to Claret vs no protection

Debris capture in all deployed devices

Evidence of effect on number and size of MRI lesions (with ~65% MRI follow up...

Some suggestion that neurocognitive decline ameliorated



Van Mieghem et al Eurointervention 2016;12:499-507

CLEAN-TAVI

100 patient, single-centre RCT

Randomised to Claret vs no Claret

Reduction in new MRI lesion volume and number

no data on neurocognitive improvement

Neurological Outcome

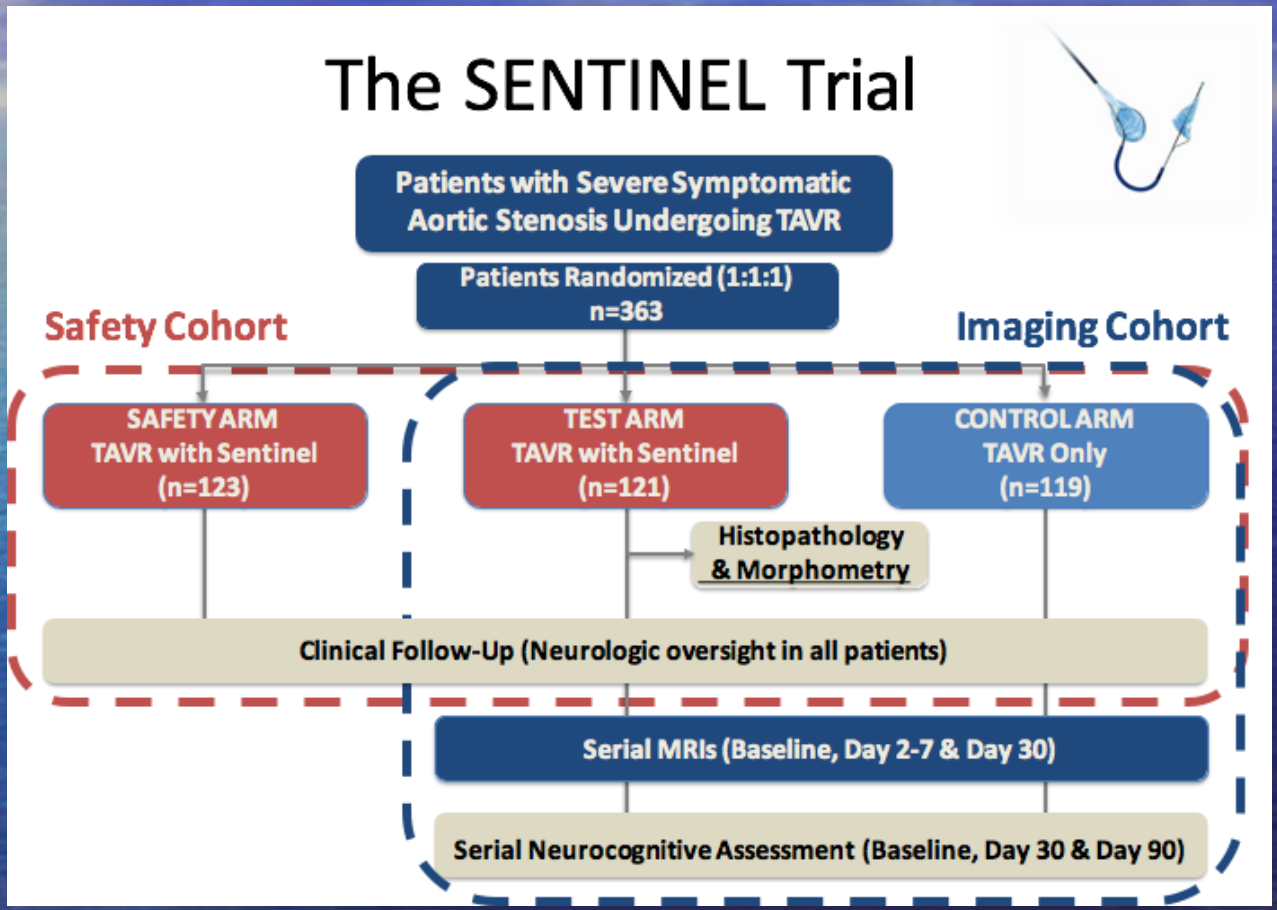
intention-to-treat		cumulative	2 days (No, %)	7 days (No, %)	30 days (No, %)
Control	Any symptom	17 (34 %)	14 (28 %)	5 (10 %)	6 (12 %)
	- Ataxia	16 (32 %)	12 (24 %)	4 (8 %)	5 (10 %)
Filter	Any symptom	14 (28 %)	8 (16 %)	8 (16 %)	6 (12 %)
	- Ataxia	12 (24 %)	6 (12 %)	7 (14 %)	6 (12 %)

RR 1.379 (0.927 to 2.050), OR 2.042, p=0.175

RR 1.439 (0.963 to 2.149), OR 2.316, p=0.118

Haussig et al JAMA 2016;316:592-601

Claret Randomised data



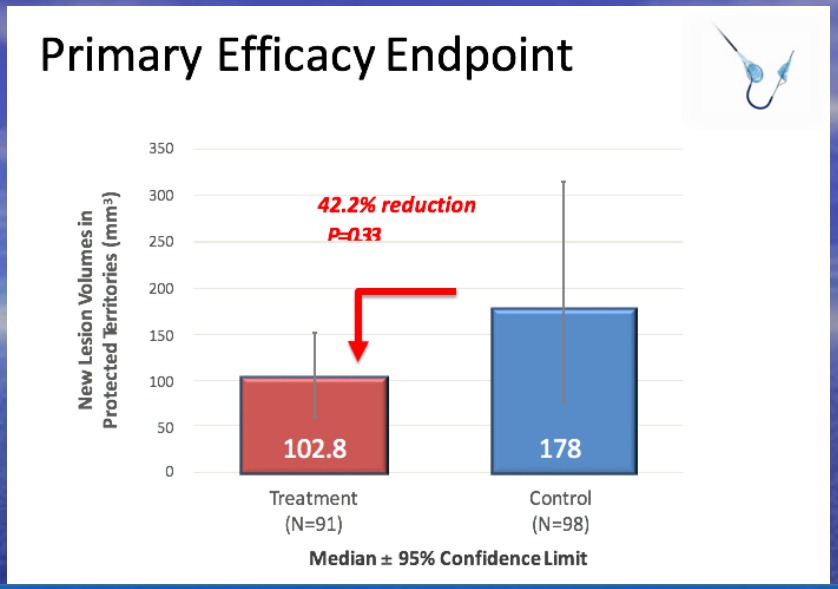
Kodali TCT 2016

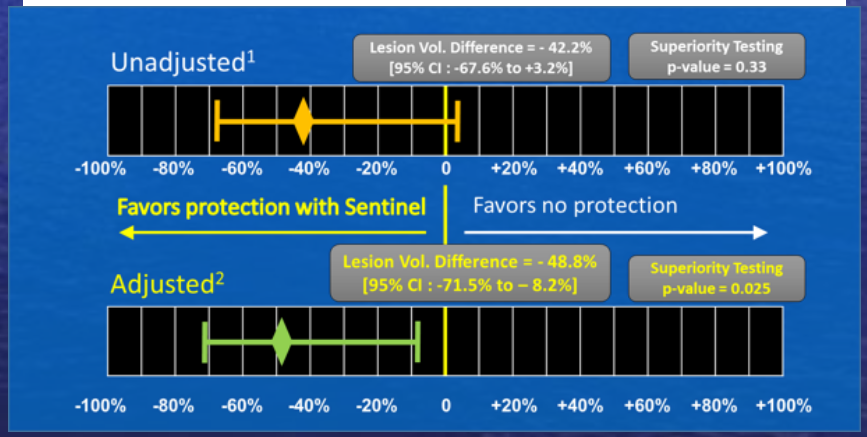
No difference in clinical stroke rates..

Despite a reduction in MRI lesion volume study failed to reach its primary end-point…

Favourable safety profile- ie no evidence of harm..

No difference in clinical stroke rates..





Kodali TCT 2016

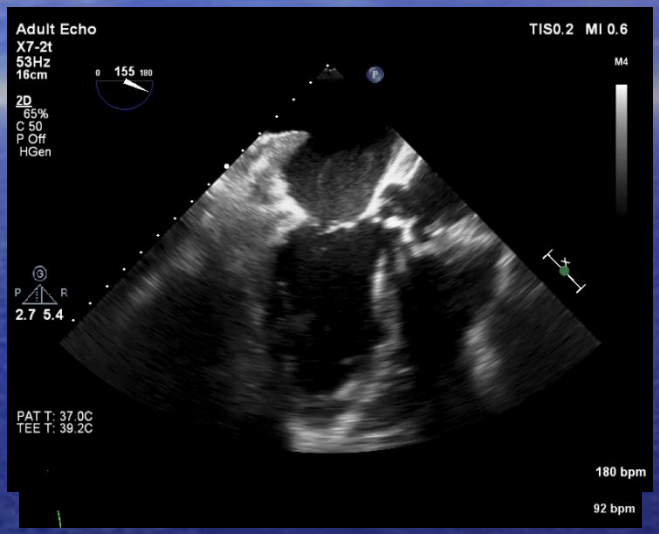
Where is it (empirically) used?

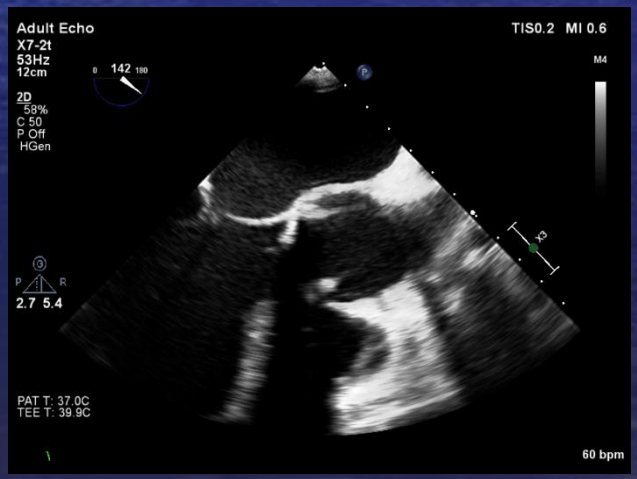
With mobile structures present on the AoV

Laminar LV thrombus in 'no option' patient

Large burden/mobile aortic atheroma..

?LA appendage clot/SEC





Summary

- Stroke continues to be a clinically relevant problem in TAVI
- 'Silent' cerebral infarcts are frequent and are shown to have an impact on cognitive function
- While initial results with cerebral protection devices promising, so far failed to be validated in powered randomized trials
- Freedom from new brain lesions should be a gold standard after TAVI?

Thank You

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