

The Silent and Apparent Neurological Injury in Transcatheter Aortic Valve Implantation Study (SANITY)

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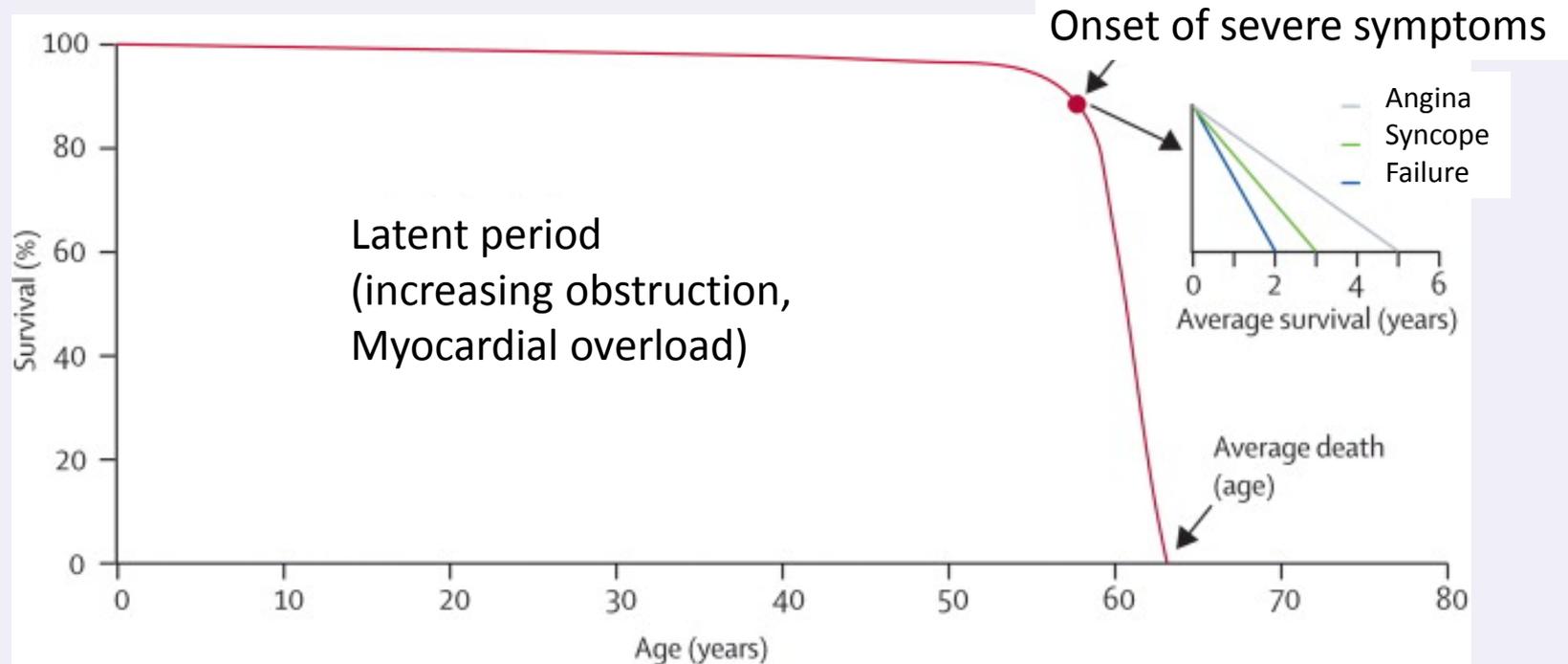


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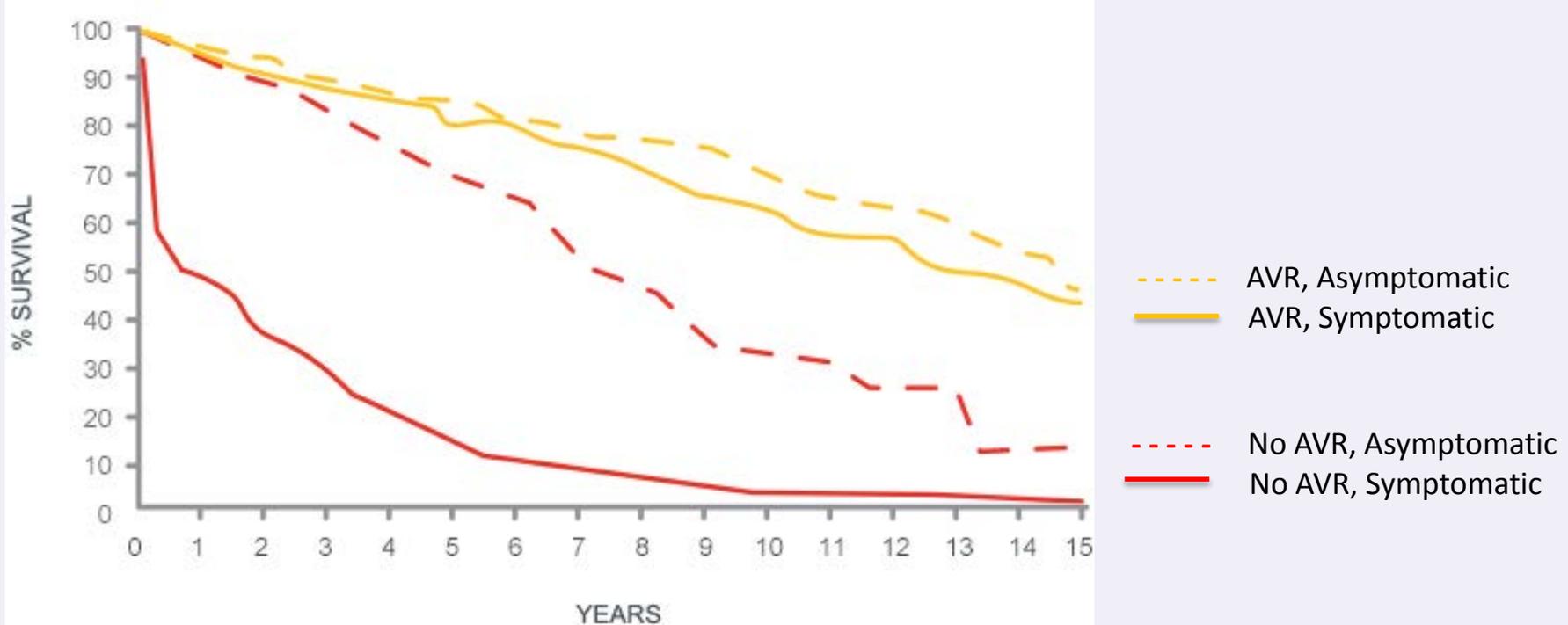
Critical Care

RESEARCH GROUP

Aortic stenosis progression

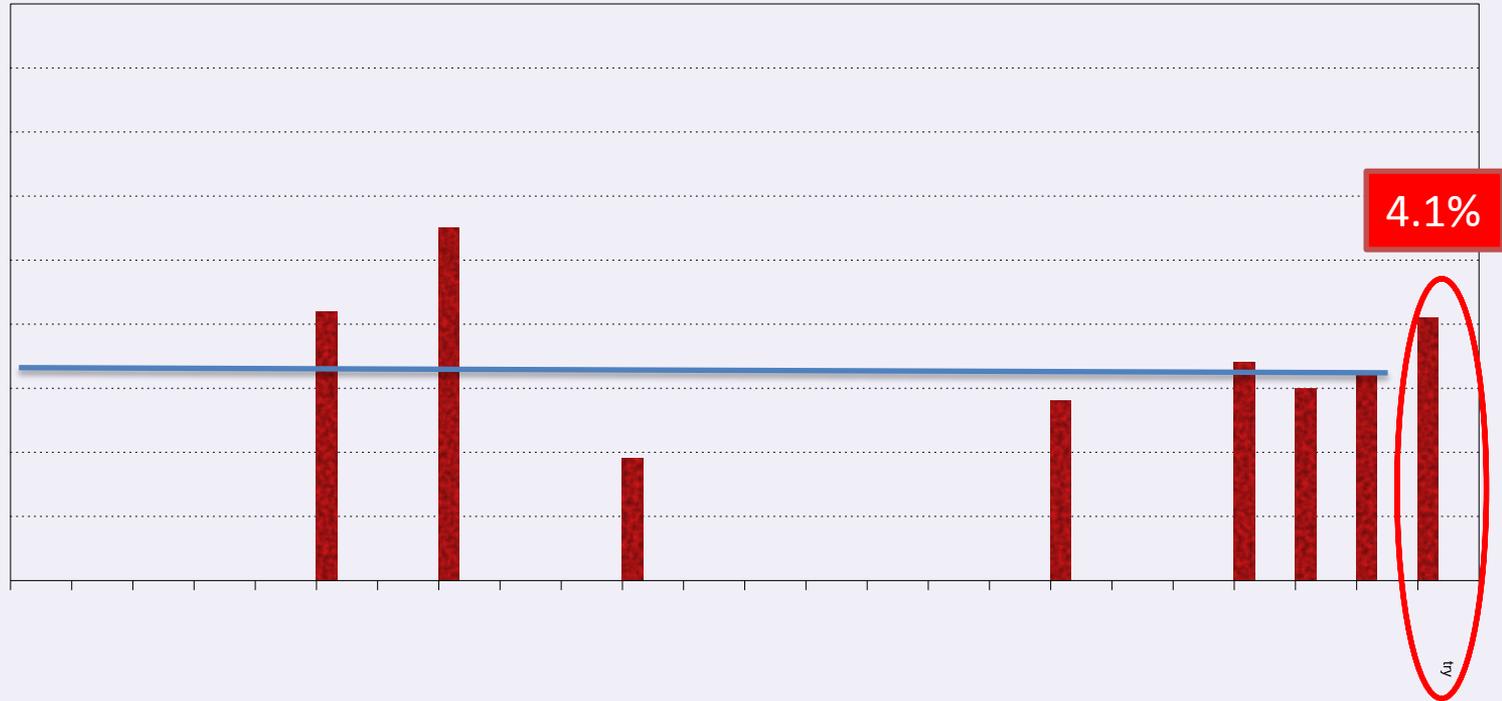


Aortic Valve Replacement – The Gold Standard



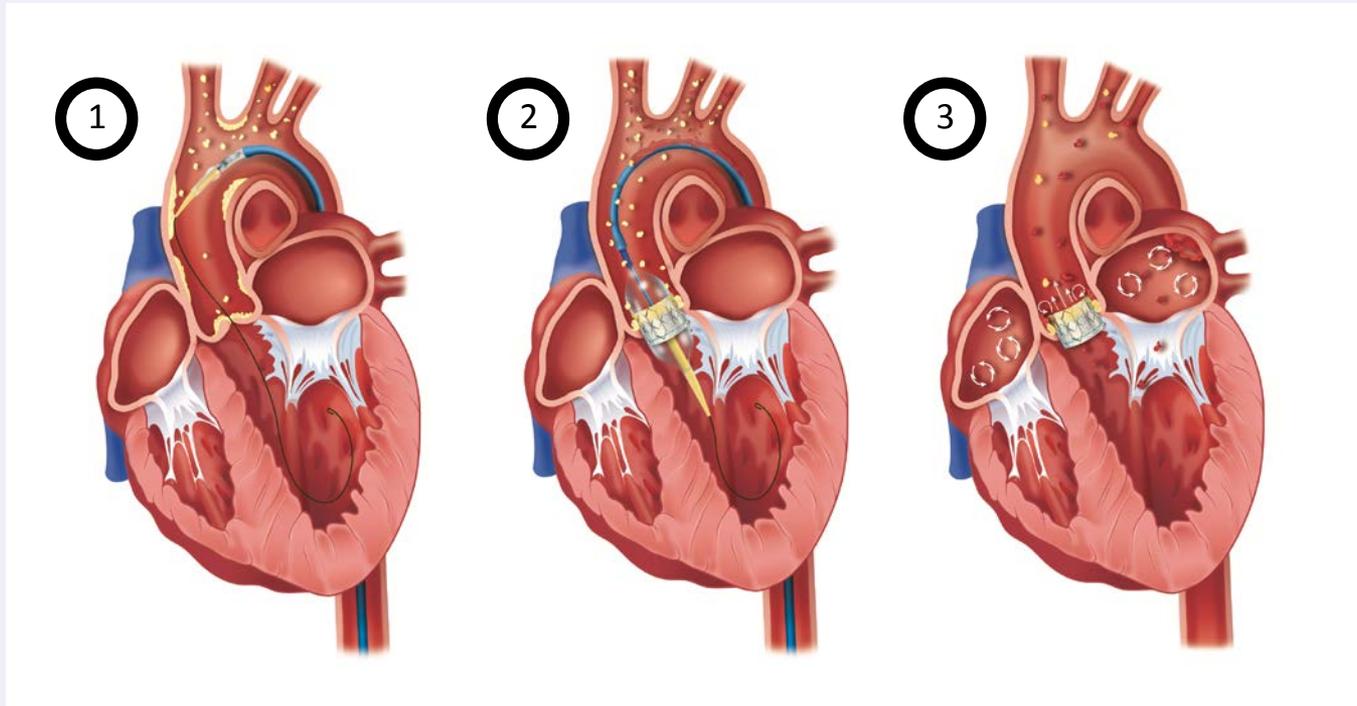
Brown, *et al.* The benefits of early valve replacement in symptomatic patients with severe aortic stenosis. *J Thorac Cardiovasc Surg.* 2008;135(2):308-315.

Incidence of Clinically-Apparent Stroke



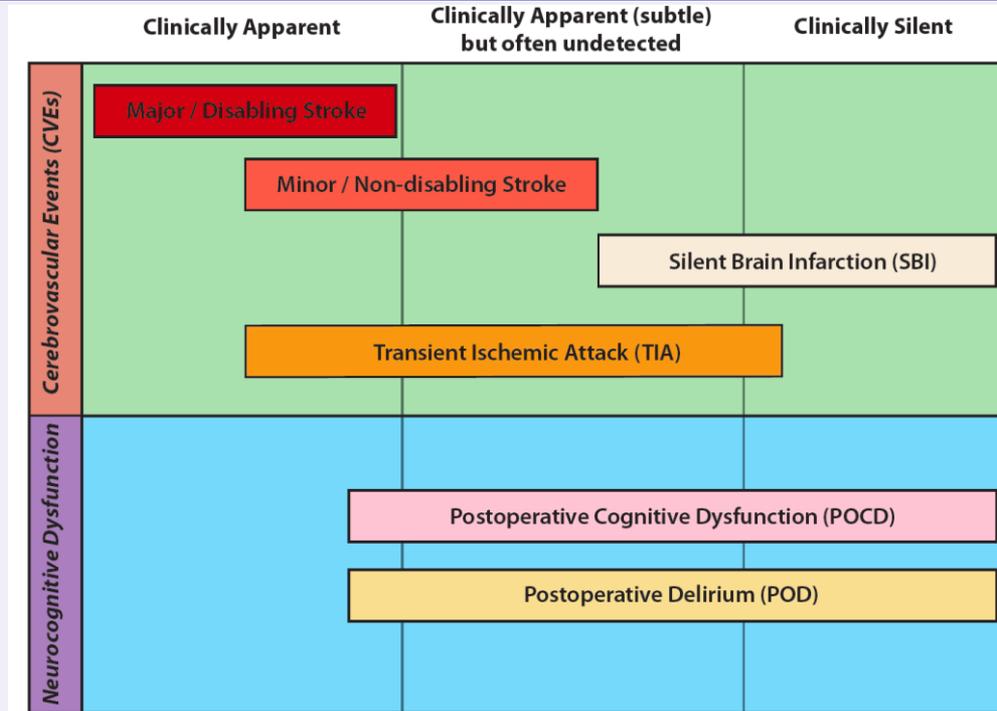
Fanning et al. Characterization of neurological injury in transcatheter aortic valve implantation (TAVI): How clear is the picture? *Circulation*. 2014;129:504-515.

Neurologic insult may result from embolisation



Fanning et al. Characterization of neurological injury in transcatheter aortic valve Implantation (TAVI): How clear is the picture? *Circulation*. 2014;129:504-515.

Clinically apparent stroke is only the 'tip of the iceberg' that is neurological injury



Fanning et al. The Silent and apparent neurological injury in transcatheter aortic valve Implantation study (SANITY): concept, design and rationale. *BMC Cardiovasc Disord.* 2014;14:45.

Purpose

Aim 1

Objectively characterise the neurological injury associated with TAVI in the modern-era

Aim 2

Identify predictive risk factors for the occurrence of neurological injury

Aim 3

Identify the prognostic significance of subclinical

SANITY Study Methodology

Design

- Prospective
- Observational

Cohort

- Undergoing TAVI *with*
- Edwards SAPIEN XT Valve *and*
- under general anesthesia

Eligibility

- Able to consent (HREC/12/QPCH/291)
- Capacity to undergo all assessments

Assessment Methodology



Clinical

- ① Risk assessment
- ② National Institute of Health Stroke Scale (NIHSS)
- ③ Montreal cognitive assessment (MoCA)
- ④ Confusion Assessment Method (CAM)
- ⑤ Functional assessment
 - a. 6-minute walk distance (6MWD)
 - b. 5 meter gait speed
- ⑥ Quality of Life
 - a. Kansas City Cardiomyopathy Questionnaire (KCCQ)
 - b. EuroQOL



Radiological



Intraoperative
Monitoring

Assessment Methodology



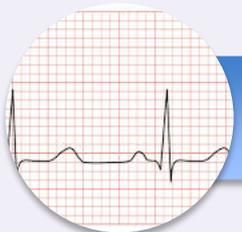
Clinical

- ① Magnetic Resonance Imaging (Brain)
 - a. Baseline
 - b. Day 3 post procedure



Radiological

- ② Carotid Duplex Ultrasound Scans
- ③ Computed Tomography Chest (non-contrast)
- ④ Echocardiography



Intraoperative
Monitoring

Assessment Methodology



Clinical

① Cerebral oximetry (INVOS™ 5100)



Radiological

② Telemetry
a. Intra-operative
b. 48 hours post-operative



Intraoperative
Monitoring

③ Invasive haemodynamic monitoring

Endpoints

Primary

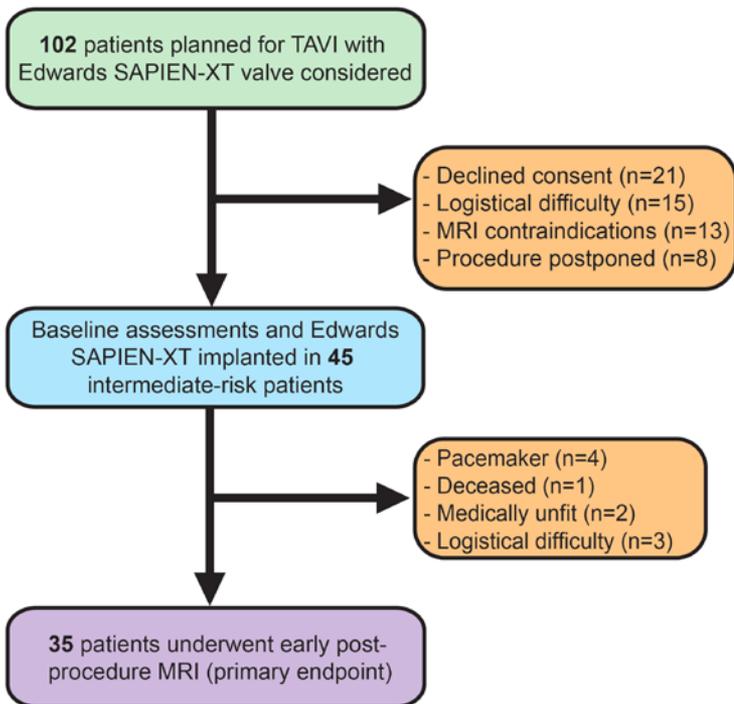
New ischemic lesions on day 3 \pm 1 post-procedure MRI scan

Secondary

Incidence of clinically apparent neurological injury reported as:

- 1) Cerebrovascular events;
- 2) Captured episodes of delirium;
- 3) Cognitive impairment

Baseline Patient Characteristics

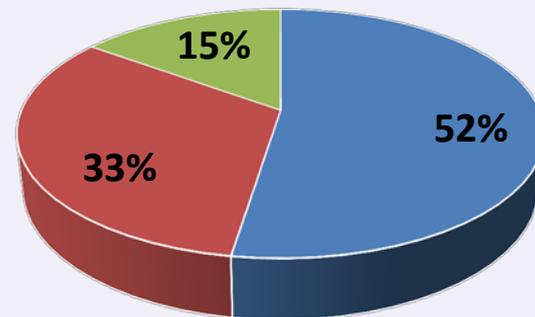


Characteristic	Measure
Number recruited (n)	45
Age, years (\pm SD)	82 (\pm 7)
Female, n (%)	26 (58%)
BMI, kg/m ² (\pm SD)	29 (\pm 7)
EuroSCORE II, % (\pm SD)	6.5 (\pm 6)
STS Score, % (\pm SD)	6.3 (\pm 3.5)
Significant carotid disease, n (%)	12 (27%)
Pre-existing neurological disease, n (%)	7 (16%)
Preoperative LVEF, % (\pm SD)	58 (\pm 14)

Procedural Characteristics

Procedural characteristic	Measure
Procedure success, n (%)	43 (96%)
Procedure duration, min (\pm SD)	70 (\pm 18)
Rapid ventricular pacing duration, sec (\pm SD)	30 (\pm 16)
Contrast volume, mL (\pm SD)	147 (\pm 45)
Fluoroscopy time, min (\pm SD)	14 (\pm 9)
ACT level at deployment	332 (\pm 50)

Access approach



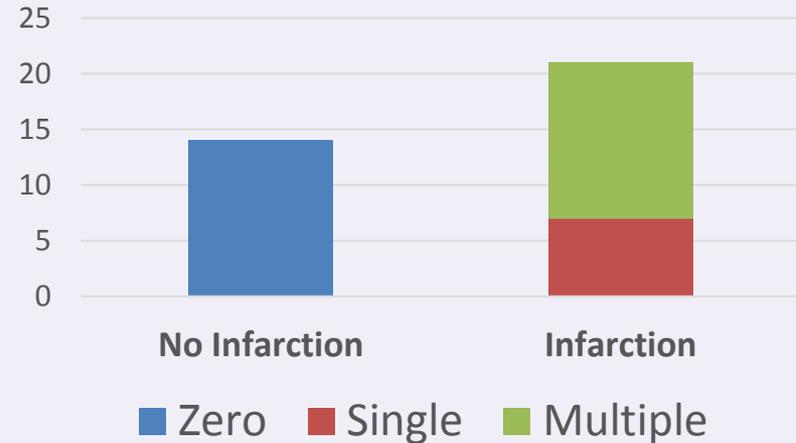
Clinically Apparent Adverse Events

Adverse events	Measure	Neurological events	Measure
Mortality	1 (2%)	TIA	0 (0%)
Myocardial Infarction	0 (0%)	Major / disabling stroke	0 (0%)
Life-threatening bleeding	1 (2%)	Minor / non-disabling stroke	1 (2%)
Major bleeding	0 (0%)	POCD	2 (4.4%)
Pacemaker implantation	4 (9%)	POD	1 (2%)
Cardiac re-intervention	1 (2%)		

Neurological Injury Assessment (Day 3)

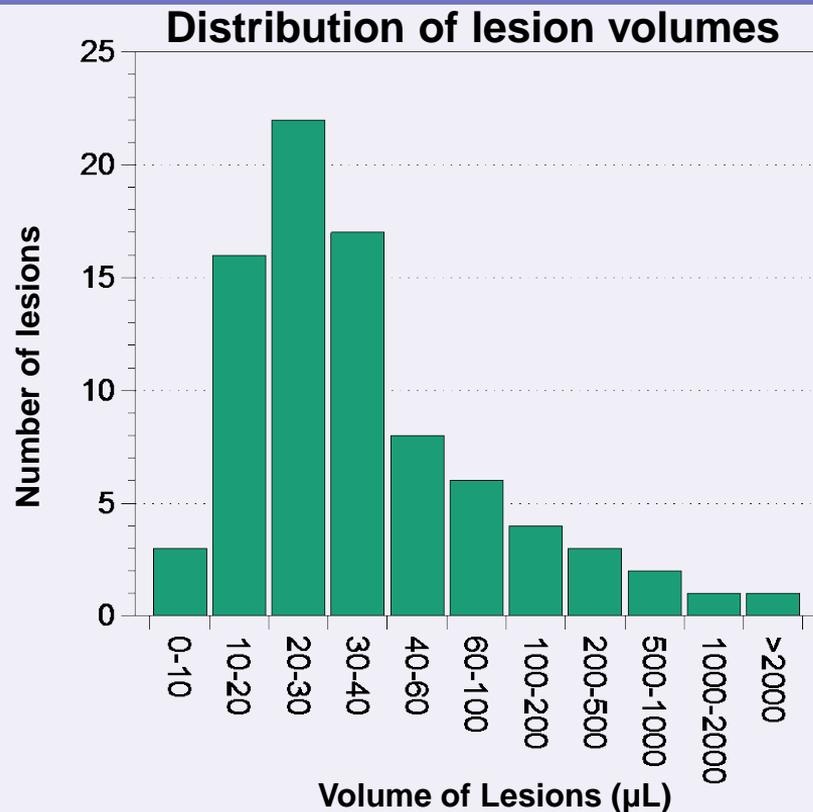
MRI Assessment	Measure
Patients with DWI lesions, n (%)	21 (60%)
- <i>Single lesion</i>	7 (20%)
- <i>Multiple lesions</i>	14 (40%)
Median(\pm IQR) lesions / patient	1 (\pm 3)
Median(\pm IQR) volume / lesion	24 (\pm 19)

Participants With vs. Without Infarction



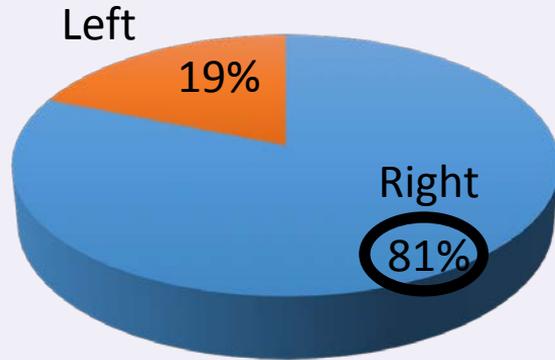
Magnetic Resonance Imaging Assessment (Day 3)

MRI Assessment	Measure
Patients with DWI lesions, n (%)	21 (60%)
- <i>Single lesion</i>	7 (20%)
- <i>Multiple lesions</i>	14 (40%)
Median(\pm IQR) lesions / patient	1 (\pm 3)
Median(\pm IQR) volume / lesion	24 (\pm 19)



Distribution of Lesions: Vascular Territory

Hemisphere

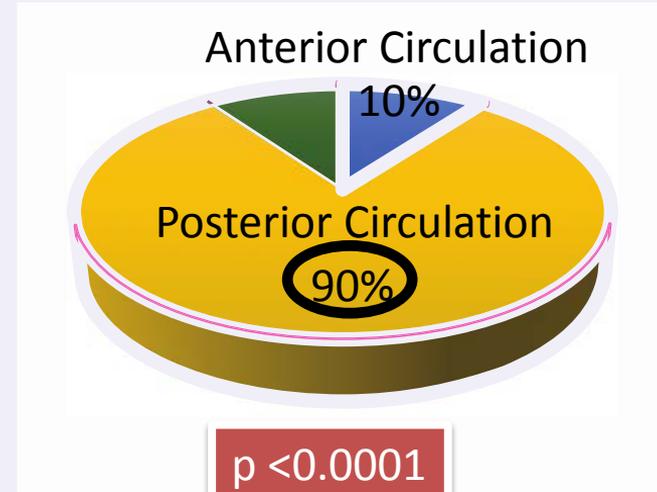


50:50

$p < 0.0001$

■ Right ■ Left

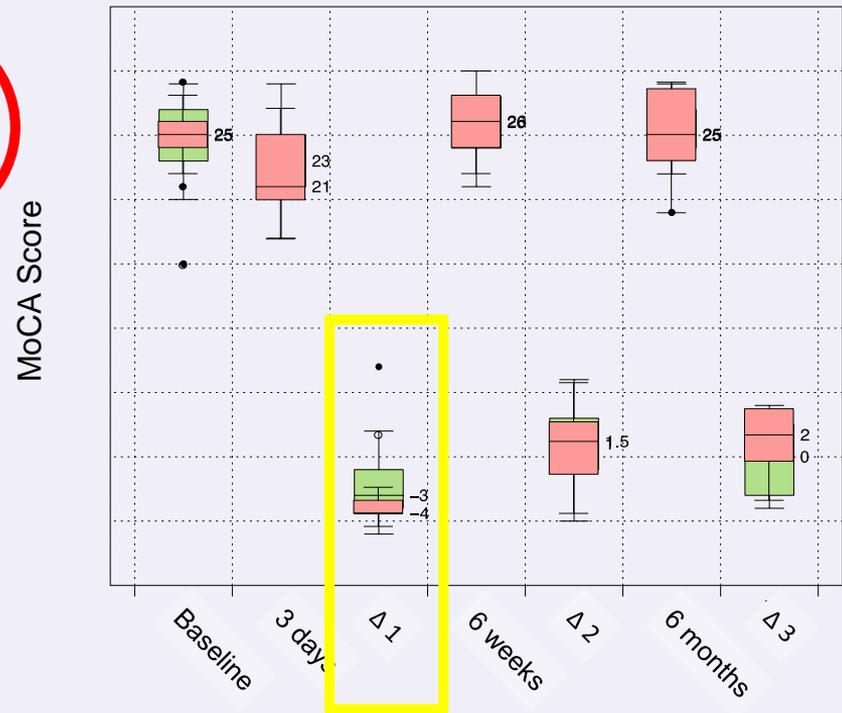
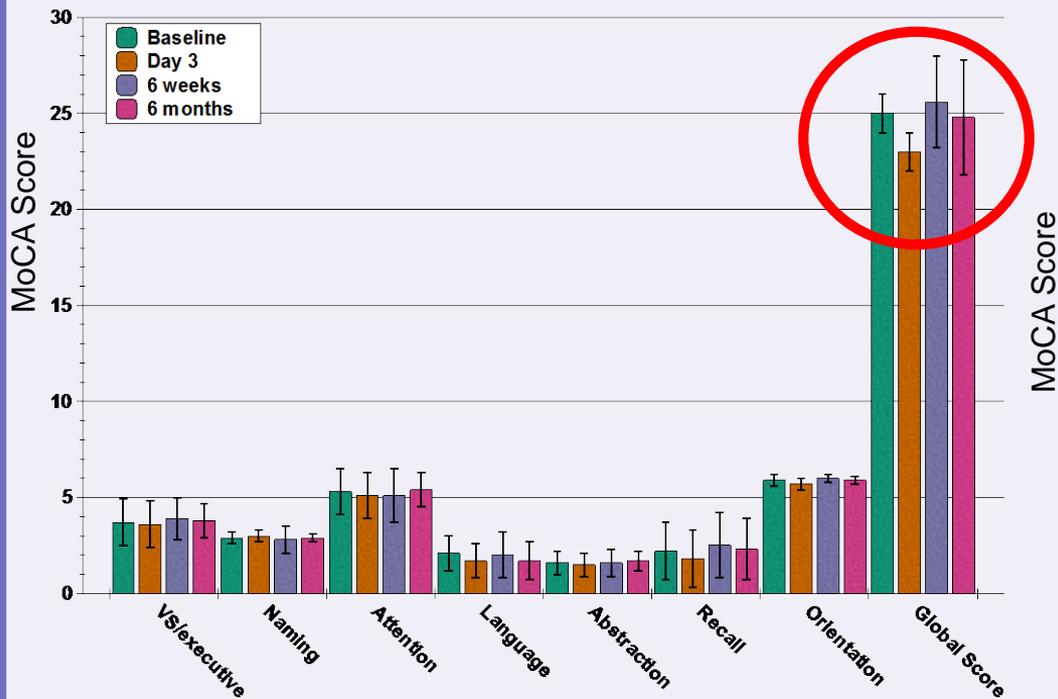
Vascular Territory



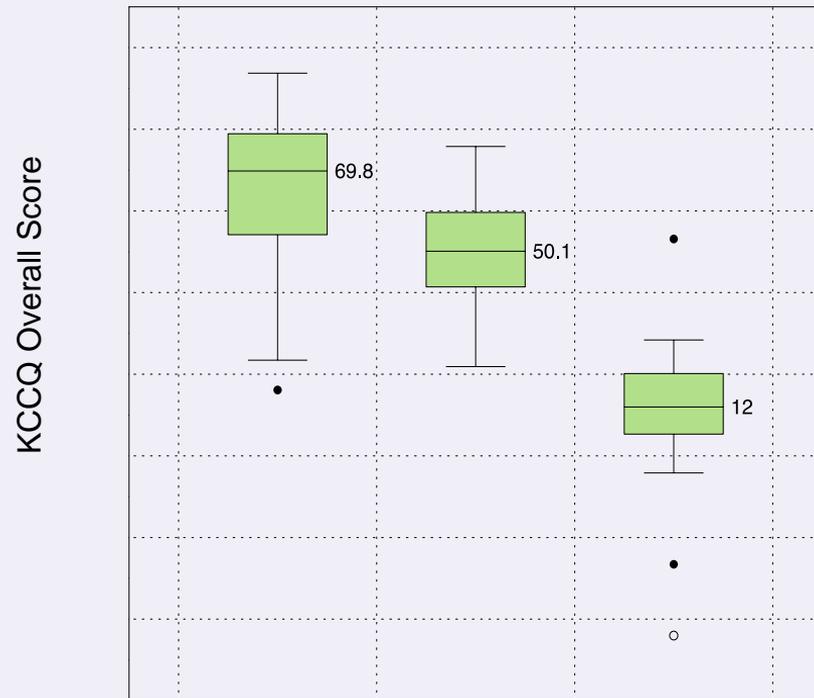
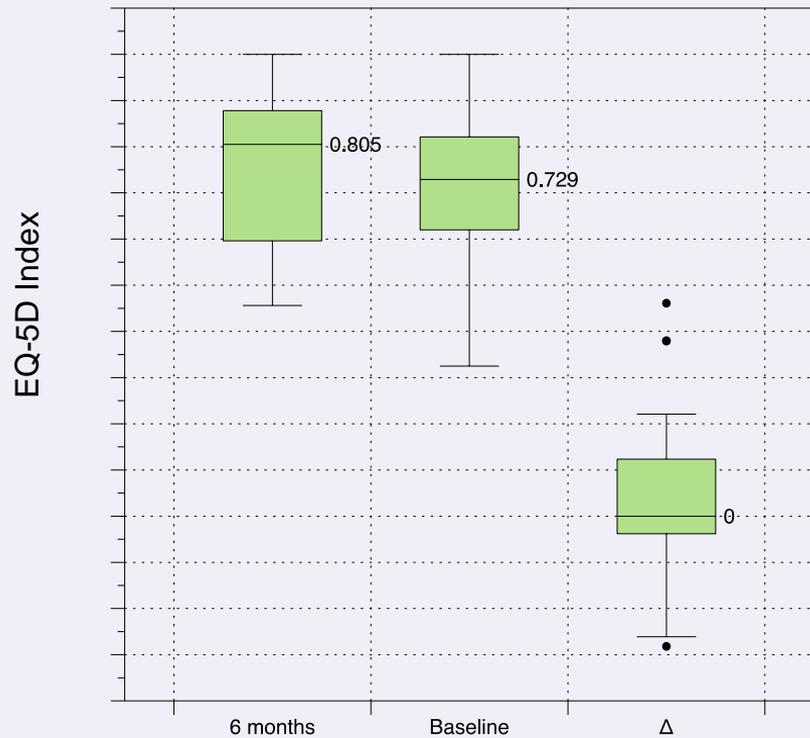
$p < 0.0001$

■ ACA ■ MCA ■ PCA ■ Vertebrobasilar

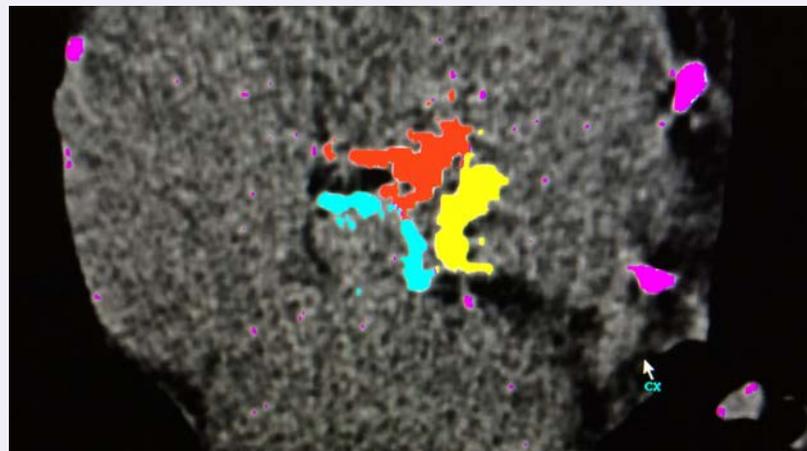
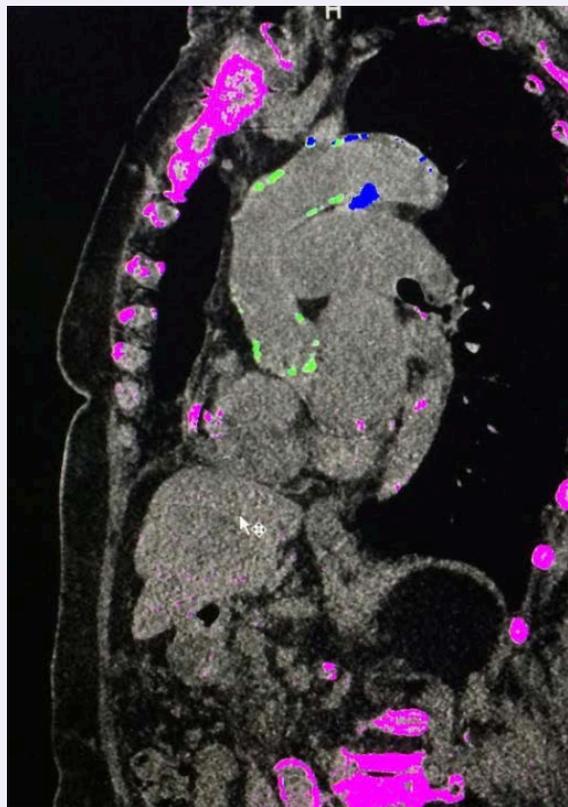
Montreal Cognitive Assessment (MoCA)



Quality of Life

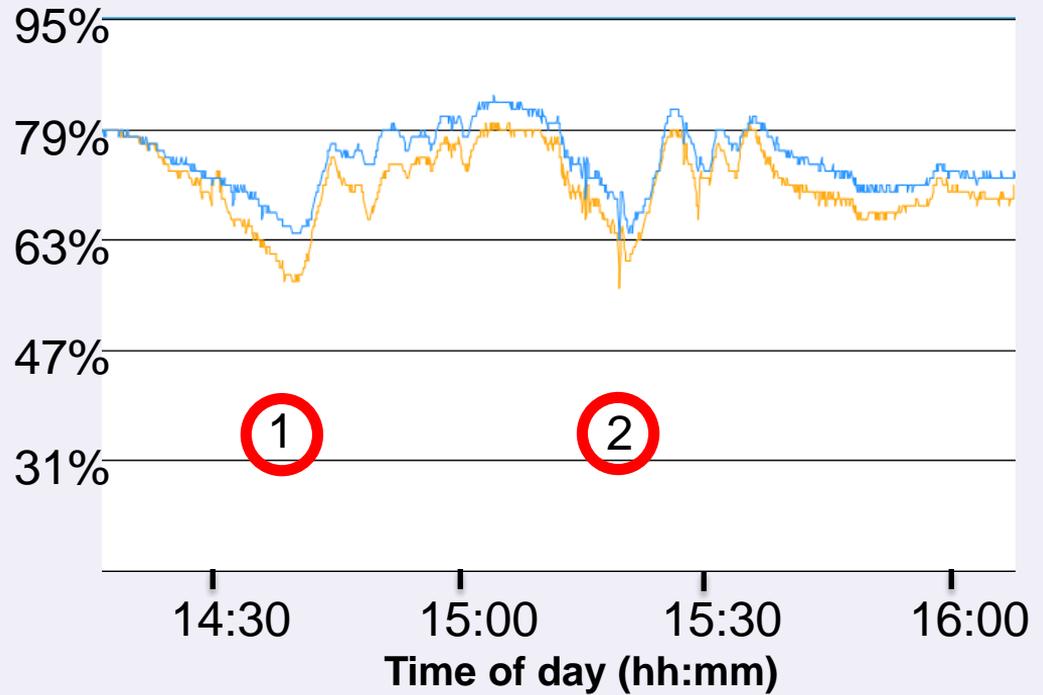


CT-detected aortic calcification

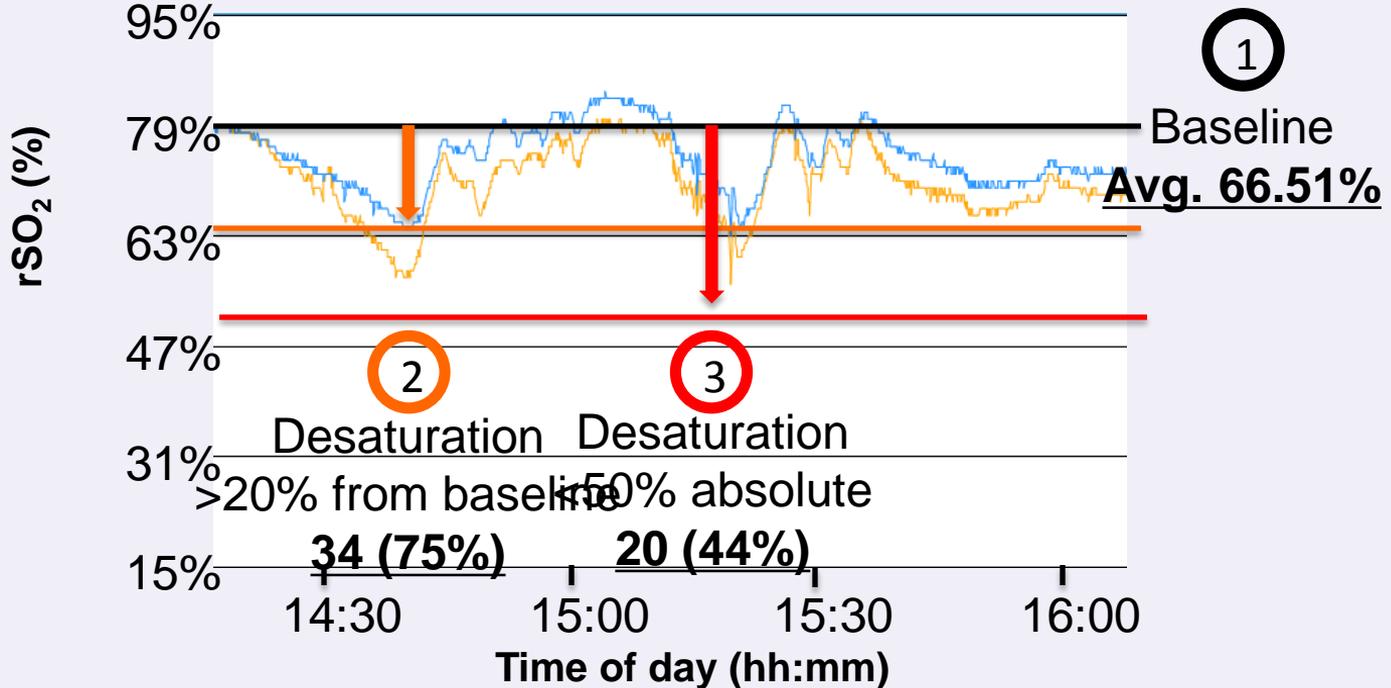


Location	Calcification score (95% CI)
Aortic valve leaflet	2089.9 (1725.2, 2452.6)
Proximal aorta	2854.15 (1735.4, 3972.9)
Total	4871.17 (3693.4, 6049.0)

Cerebral oximetry



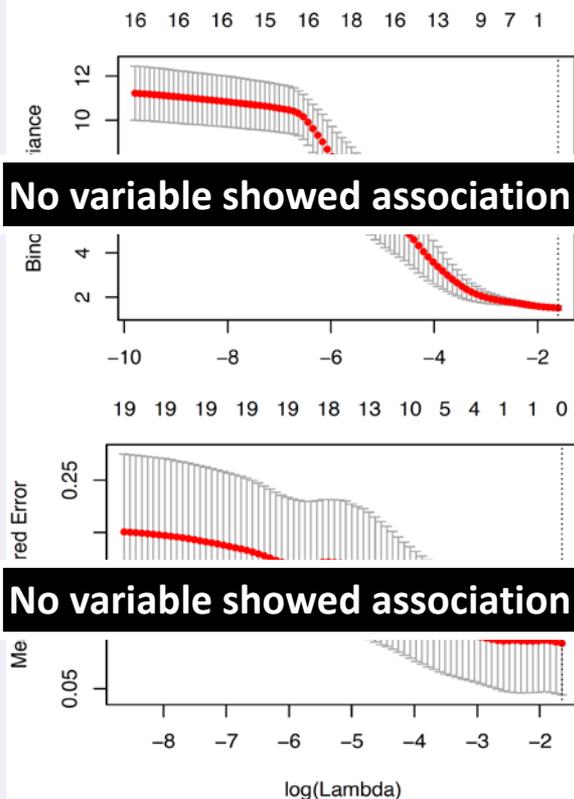
Cerebral oximetry



Logistic Regression: Presence of DWI lesions

Cross-validated error:

1. Binary outcome DWI lesions



2. DWI lesion volume

- Categorical predictors:
 - Gender
 - Smoking
 - History of: stroke, TIA, HTN, CKD, IHD, AF, carotid stenosis
 - Post-implantation maneuvers
 - Rapid ventricular pacing duration
- Continuous predictors:
 - Age
 - BMI
 - Risk scores (STS, Log EuroSCORE, EuroSCORE 2)
 - Baseline ejection fraction
 - Baseline cognition (MoCA)
 - Calcification score (Total)

Summary of findings

- **Incidence:** Neurologic injury is a common occurrence following TAVI (60%) irrespective of risk stratification
- **Distribution:** Posterior circulation is particularly vulnerable.
- **Implications of neurologic injury:** The presence of DWI+ lesions is associated with reduced early cognition
- **Predictors of neurologic injury:** Significant cerebral hypoperfusion/desaturation is seen in the majority of procedures but did not correlate with neurological injury
- Severe calcification is seen in the majority of patients but did not correlate with neurological injury

Future Direction

- Finalise analysis of **SANITY** Surgical AVR control group
- The **Australian Cerebrovascular Hazard / Insult chaLLEnging aortic Stenosis** management (**ACHILLES**) study
- **Neuroprotective strategies:**
 - **Neuro-PROTECT** study: remote ischemic preconditioning and targeted temperature management during the procedure
 - **Australian Deflector Device In TAVI (ADDIT)** trial
- Characterising the prothrombotic state associated with TAVI
- Imaging neural networks with **Connectomics** to objectively assess cognition
- **Rheology** of cardiac emboli

Acknowledgements



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