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

**Jonathon Fanning**, Allan Wesley, Darren Walters, Eamonn Eeles, David Platts, John Fraser

The University of Queensland, Brisbane, Queensland, AUSTRALIA
The Critical Care Research Group, The Prince Charles Hospital, Brisbane, AUSTRALIA
Heart & Lung Institute, The Prince Charles Hospital, Brisbane, AUSTRALIA
Aortic stenosis progression

Latent period
(increasing obstruction, Myocardial overload)

Onset of severe symptoms

Aortic Valve Replacement – The Gold Standard

Incidence of Clinically-Apparent Stroke

Neurologic insult may result from embolisation

Clinically apparent stroke is only the ‘tip of the iceberg’ that is neurological injury.
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

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 Caridiomyopathy Questionnaire (KCCQ)
   b. EuroQOL
Assessment Methodology

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

② Carotid Duplex Ultrasound Scans

③ Computed Tomography Chest (non-contrast)

④ Echocardiography
Assessment Methodology

① Cerebral oximetry (INVOS™ 5100)

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

③ Invasive haemodynamic monitoring
Endpoints

Primary

New ischemic lesions on day $3\pm1$ 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

102 patients planned for TAVI with Edwards SAPIEN-XT valve considered

- Declined consent (n=21)
- Logistical difficulty (n=15)
- MRI contraindications (n=13)
- Procedure postponed (n=8)

Baseline assessments and Edwards SAPIEN-XT implanted in 45 intermediate-risk patients

- Pacemaker (n=4)
- Deceased (n=1)
- Medically unfit (n=2)
- Logistical difficulty (n=3)

35 patients underwent early post-procedure MRI (primary endpoint)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number recruited (n)</td>
<td>45</td>
</tr>
<tr>
<td>Age, years (±SD)</td>
<td>82 (±7)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>26 (58%)</td>
</tr>
<tr>
<td>BMI, kg/m² (±SD)</td>
<td>29 (±7)</td>
</tr>
<tr>
<td>EuroSCORE II, % (±SD)</td>
<td>6.5 (±6)</td>
</tr>
<tr>
<td>STS Score, % (±SD)</td>
<td>6.3 (±3.5)</td>
</tr>
<tr>
<td>Significant carotid disease, n (%)</td>
<td>12 (27%)</td>
</tr>
<tr>
<td>Pre-existing neurological disease, n (%)</td>
<td>7 (16%)</td>
</tr>
<tr>
<td>Preoperative LVEF, % (±SD)</td>
<td>58 (±14)</td>
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## Procedural Characteristics

<table>
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<th>Procedural characteristic</th>
<th>Measure</th>
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<tbody>
<tr>
<td>Procedure success, n (%)</td>
<td>43 (96%)</td>
</tr>
<tr>
<td>Procedure duration, min (± SD)</td>
<td>70 (± 18)</td>
</tr>
<tr>
<td>Rapid ventricular pacing duration, sec (± SD)</td>
<td>30 (± 16)</td>
</tr>
<tr>
<td>Contrast volume, mL (± SD)</td>
<td>147 (± 45)</td>
</tr>
<tr>
<td>Fluoroscopy time, min (± SD)</td>
<td>14 (± 9)</td>
</tr>
<tr>
<td>ACT level at deployment</td>
<td>332 (± 50)</td>
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### Access approach

- Transfemoral: 52%
- Transaortic: 33%
- Transapical: 15%
Clinically Apparent Adverse Events

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Measure</th>
<th></th>
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<tbody>
<tr>
<td>Mortality</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Life-threatening bleeding</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Pacemaker implantation</td>
<td>4 (9%)</td>
<td></td>
</tr>
<tr>
<td>Cardiac re-intervention</td>
<td>1 (2%)</td>
<td></td>
</tr>
</tbody>
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<table>
<thead>
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<th>Neurological events</th>
<th>Measure</th>
<th></th>
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<tbody>
<tr>
<td>TIA</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Major / disabling stroke</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Minor / non-disabling stroke</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>POCD</td>
<td>2 (4.4%)</td>
<td></td>
</tr>
<tr>
<td>POD</td>
<td>1 (2%)</td>
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Neurological Injury Assessment (Day 3)

<table>
<thead>
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<th>MRI Assessment</th>
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<tr>
<td>Patients with DWI lesions, n (%)</td>
<td>21 (60%)</td>
</tr>
<tr>
<td>- Single lesion</td>
<td>7 (20%)</td>
</tr>
<tr>
<td>- Multiple lesions</td>
<td>14 (40%)</td>
</tr>
<tr>
<td>Median(±IQR) lesions / patient</td>
<td>1 (±3)</td>
</tr>
<tr>
<td>Median(±IQR) volume / lesion</td>
<td>24 (±19)</td>
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Participants With vs. Without Infarction

- No Infarction
  - Zero
- Infarction
  - Single
  - Multiple
### MRI Assessment Measure

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#### Distribution of lesion volumes

![Graph showing the distribution of lesion volumes](image)

- **Number of lesions**
- **Volume of Lesions (μL)**
- **Distribution of lesion volumes**
Distribution of Lesions: Vascular Territory

**Hemisphere**
- Right: 81%
- Left: 19%
- 50:50, p < 0.0001

**Vascular Territory**
- Anterior Circulation: 10%
- Posterior Circulation: 90%
- ACA: Green
- MCA: Blue
- PCA: Yellow
- Vertebrobasilar: Green
- p < 0.0001
Montreal Cognitive Assessment (MoCA)

MoCA Score

MoCA Score

[Graph showing MoCA scores over time and across domains]

Baseline
Day 3
6 weeks
6 months
CT-detected aortic calcification

<table>
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<tr>
<th>Location</th>
<th>Calcification score (95% CI)</th>
</tr>
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<tr>
<td>Aortic valve leaflet</td>
<td>2089.9 (1725.2, 2452.6)</td>
</tr>
<tr>
<td>Proximal aorta</td>
<td>2854.15 (1735.4, 3972.9)</td>
</tr>
<tr>
<td>Total</td>
<td>4871.17 (3693.4, 6049.0)</td>
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</table>
Logistic Regression: Presence of DWI lesions

Cross-validated error:

1. Binary outcome DWI lesions

No variable showed association

2. DWI lesion volume

No variable showed association

- 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 challengEning 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
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