

Cerebral protection device in TAVR, based on pre cta brain will reduce stroke events

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TAVI
58-100%

CAS
20-70%

AVR
48%

Cardiac Cath
3-18%

CABG
18-42%

AF Ablation
7-42%

New Ischemic Lesions are Present
in a Substantial Number
of **Patients** Undergoing
Cardiovascular Interventions with
Diffusion weighted (DWI) MRI
Estimates: 600,000 pts/year

Clinical Consequences and Brain Injury

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

Proposed Standardized Neurologic Endpoints in Cardiovascular Clinical Trials [NeuroARC]

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

— **International Multi Stakeholder Consensus.** Chairs: Baumbach, Lansky, Mack, Messé —

Interventional/Structural/ CT Surgery	Neurology/Neuroradiology/ Neuropsychology/NINDS	FDA/ARC/Pathology
<p>Andreas Baumbach John Forrest David Holmes Susheel Kodali Alexandra Lansky Axel Linke Raj Makkar Jeffrey Moses Cody Pietras Jeffrey Popma Bernard Prendergast Joachim Schofer Arie P. Kappetein Michael Mack</p>	<p>Kevin Abrams Michel Bilello Adam Brickman Jeffrey Browndyke Karen Furie David Greer Daryl Gress Ronald Lazar Steven Messé Claudia Moy Nils Petersen Ola Selnes Michael Dwyer Szilard Voros Bart van der Worp</p>	<p>FDA Andrew Farb Nicole Ibrahim John Laschinger Carlos Pena Bram Zuckerman Academic Research Consortium (ARC) Donald Cutlip Gerrit-Anne van Es Mitch Krucoff Roxana Mehran Pathology and Regulatory Semih Oktay Renu Virmani</p>

NeuroloArc applies to all CV trials

Neurologic evaluation and endpoints should be tailored to the procedure/device category

CATEGORY I <u>Primary Procedural</u> <u>Safety Measure</u>	CATEGORY II <u>Primary Procedural</u> <u>Efficacy Measure</u>	CATEGORY III <u>Primary Procedural Safety, Long-term</u> <u>Efficacy Measure</u>
<p>Devices with inherent iatrogenic embolic risk</p> <ul style="list-style-type: none">• Surgical cardiac procedures (valve replacement, CABG, dissection, aneurysm repair)• Adjunctive pharmacology	<p>Devices designed to prevent iatrogenic or spontaneous acute neurologic injury</p> <ul style="list-style-type: none">• Neuroprotection device• Cerebral temperature management devices	<p>Devices with inherent iatrogenic embolic risk and designed for prevention of spontaneous long-term risk</p> <ul style="list-style-type: none">• Atrial Fibrillation Ablation• PFO or LAA closure devices



NeuroARC Definitions and Classification Relevant to Patients, Comprehensive , Practical

Type 1: Overt CNS Injury (Acutely Symptomatic)		
Type 1a	Ischemic Stroke	Focal or multi-focal vascular territory Symptoms \geq 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 \geq 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

NeuroARC Recommended Assessments: Clinical, Functional, Anatomic Correlations

CLINICAL EVALUATIONS

Assessment:

- Stroke
- Disability
- Delirium
- Cognition*
- Quality of Life

Assessment:

- Stroke (<48 h, 3-5 days, and pre-discharge)
- Delirium (1, 3, 7 days)
- Cognition

Assessment:

- Stroke
- Disability
- Cognition*
- Quality of Life

Assessment:

- Stroke
- Disability
- Cognition
- Quality of Life

Baseline

Procedure

Discharge

30-90 days

1 year

5 years

MRI

With routine imaging:

MRI at 2-7 days

Without routine imaging:

MRI if neurologic symptoms or delirium

MRI

MRI if neurologic symptoms

Recommended

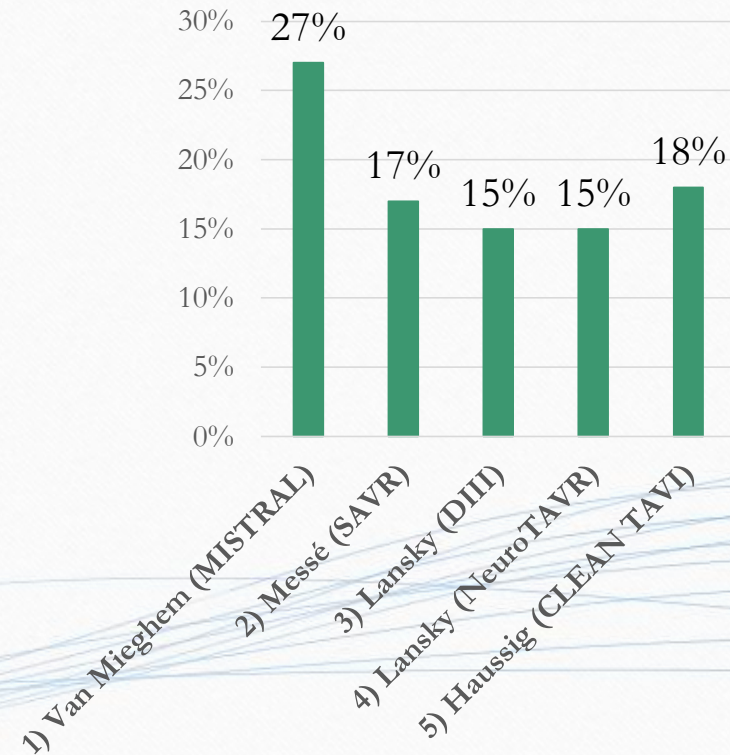
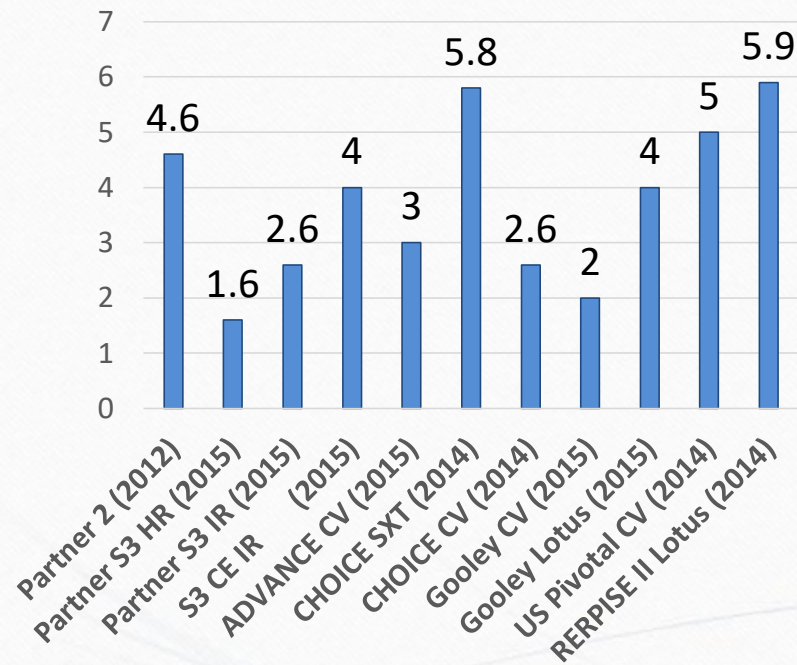
IMAGING EVALUATIONS

Optional

Stroke is common and underreported after TAVR □

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

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



¹Van Mieghem NM, EuroIntervention. 2016;12:499. ²Messe S, Circulation. 2014;129:2253. ³Lansky AJ, Eur Heart J. 2015; 36:2070.

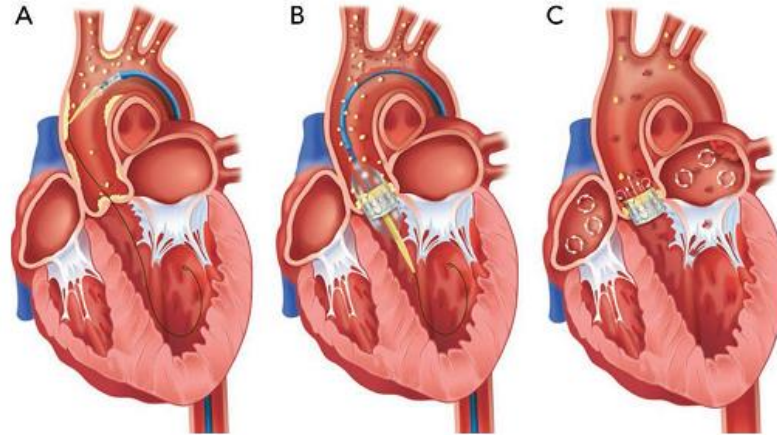
⁴Lansky AJ, PCR London Valves 2015, AJC 2016 (in press). ⁵Haussig S, JAMA. 2016;316:592.

Complications

- Migration of Valve
- Access site
- AV block
- Shock
- Bleeding
- Urgent SAVR
- Coronary artery closure

Disruption of calcium, plaque and thrombus

Figure 1: Aetiology of Embolisation Secondary to Transcatheter Aortic Valve Implantation



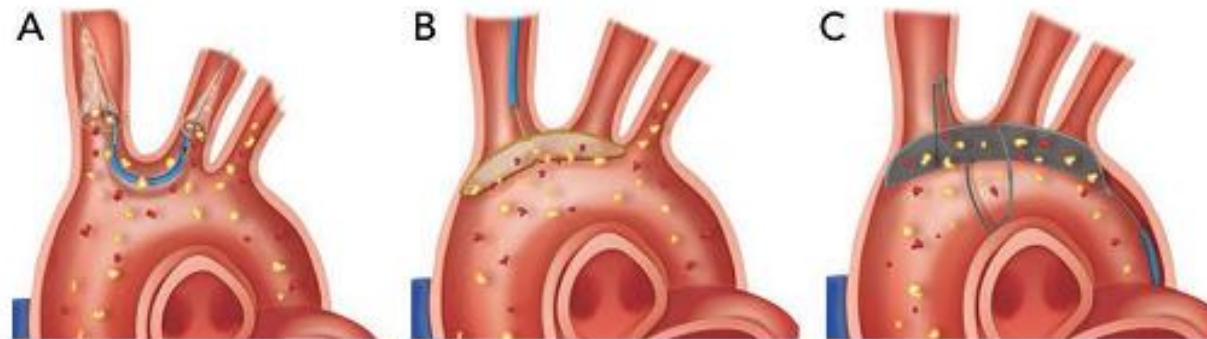
(A) and (B) Acute embolisation. Disruption of calcific/atheromatous plaques and valve/vascular tissue associated with: (A) the passage of guide wires and large-bore catheters and during valvuloplasty and device delivery; and (B) device positioning and implantation with thrombus forming on the catheter. (C) Subacute embolisation. Persistent nidus of calcium on the native valve leaflets provides a source for further calcific embolisation: thrombus formation secondary to structural changes to native leaflets, the presence of a prosthetic device and altered rheology attributable to both the apposition of native leaflets to the aortic wall and atrial fibrillation. Adapted from Fanning et al., 2014²⁸ with permission from Wolters Kluwer Health, Inc, © 2014.

Prevent Stroke by Filter device

- Claret device
- Embrella
- Trigaurd

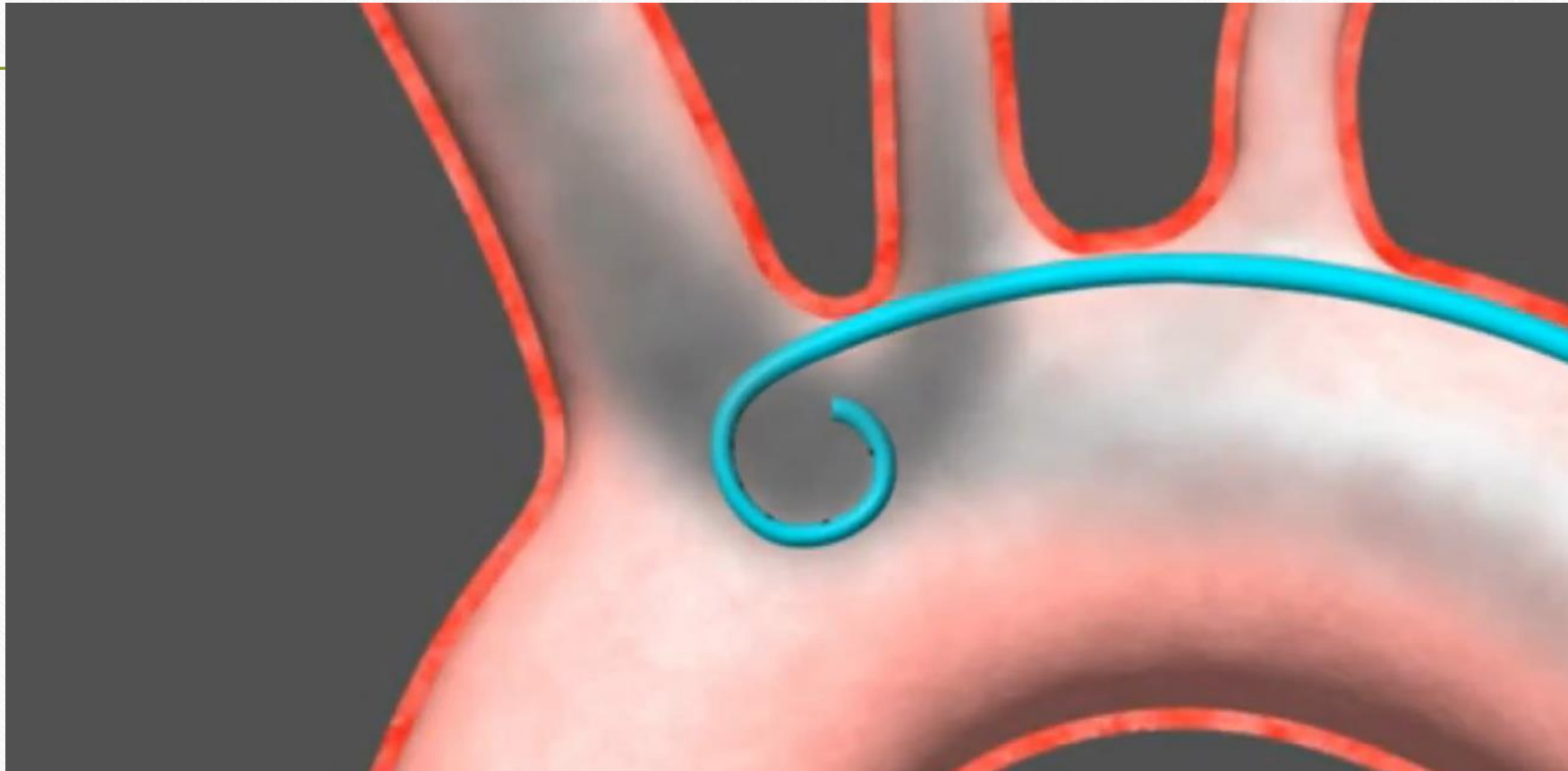
Various embolic protection devices

Figure 3: Embolic Protection Devices



(A) Montage™ 2 Capture Device (Claret); (B) Embrella Embolic Deflector System (Edwards Lifesciences); and (C) TriGuard™ Cerebral Protection Device (Keystone Heart). Adapted from Fanning et al., 2014²⁵ with permission from Wolters Kluwer Health, Inc, © 2014.

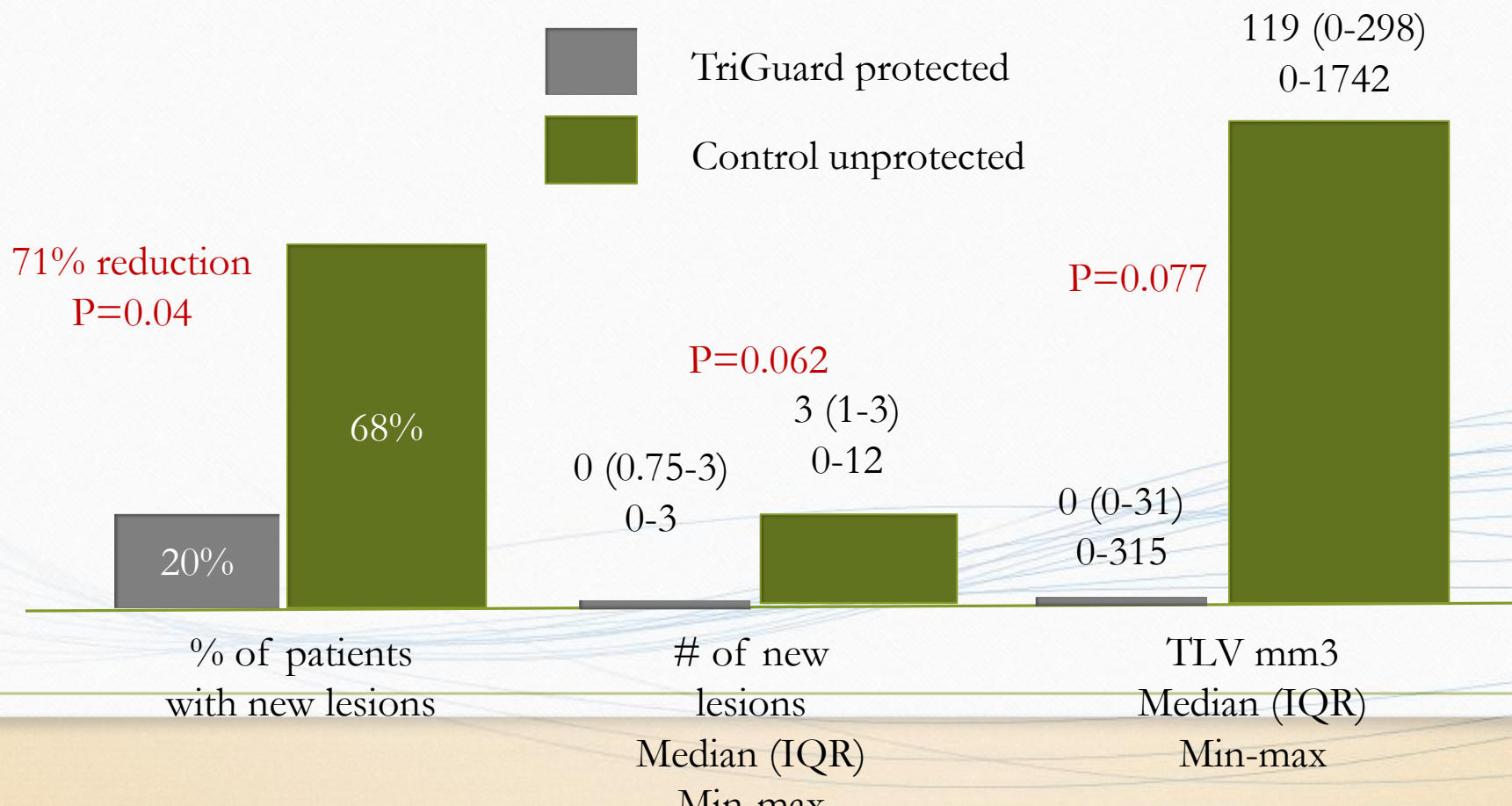
Claret filter



TriGuard Device for Cerebral Embolic Protection During Trans catheter Aortic Valve Replacement: A Multicenter Real-World Experience

Masieh Abawi, Ermela Yzeiraj; Adriaan Kraaijeveld,; Michiel Voskuil,; Pieter A. Doevendans; Joachim Schofer; Pieter R. Stella

51pts with TG vs 150 controls, Logistic EuroSCORE 12.6 ± 8.3 , Stroke rate was 0% in both groups



Debris during TAVR

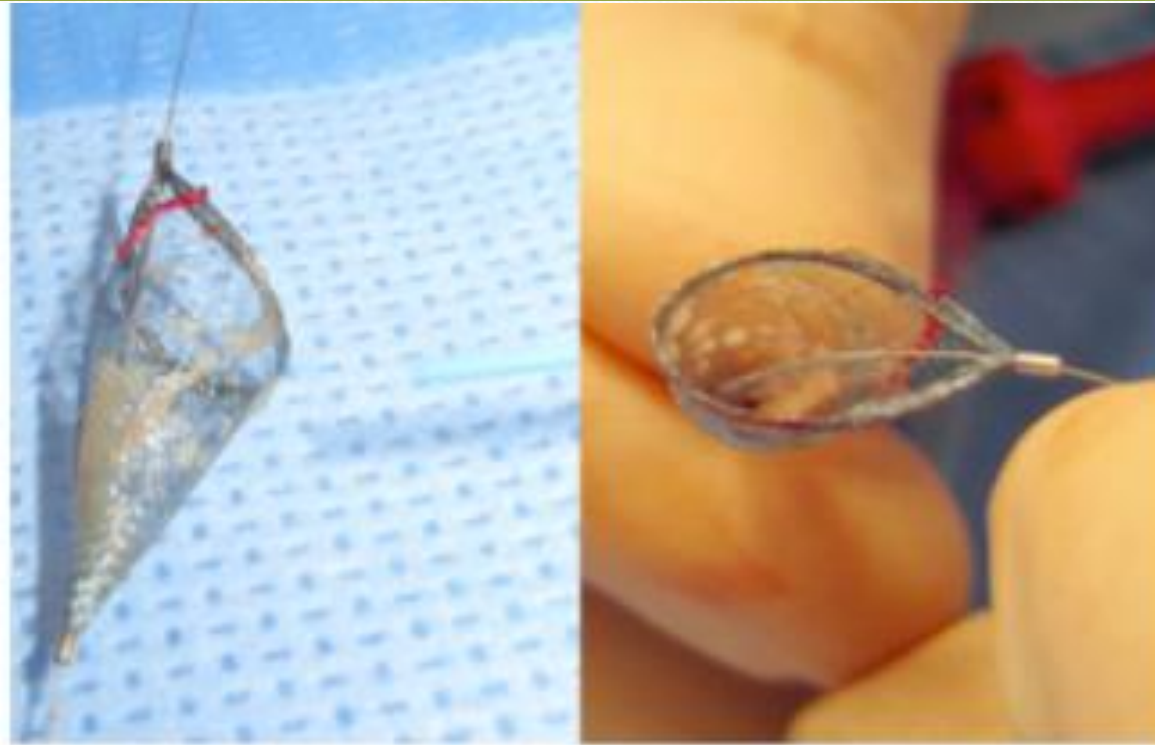
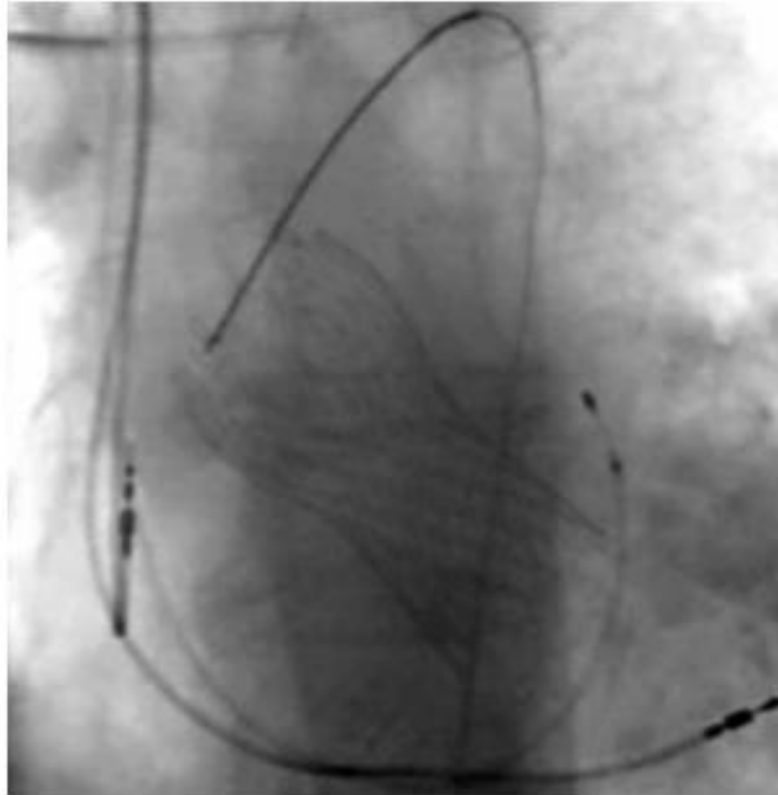


Image 1: Debris liberated during TAVI which has been captured by an

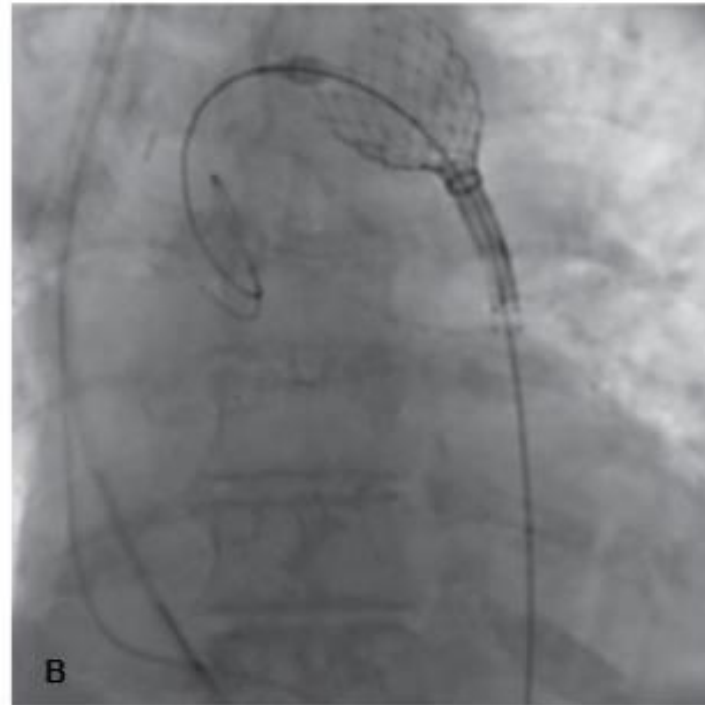
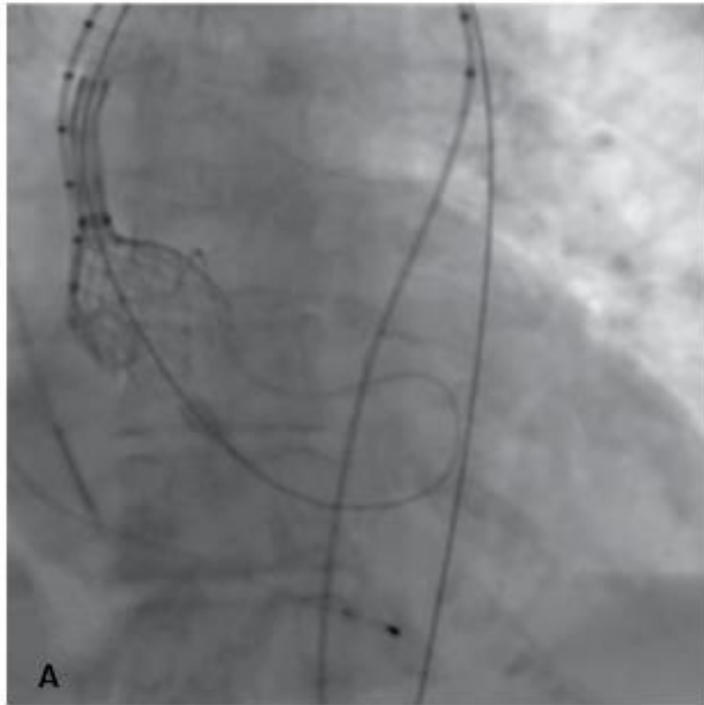
Missing of target area or Migration

- It will be major setback which can cause acute stroke.
- Shock.
- Unnecessary bleeding.
- Escalate the treatment cost.
- Increases hospital stay.

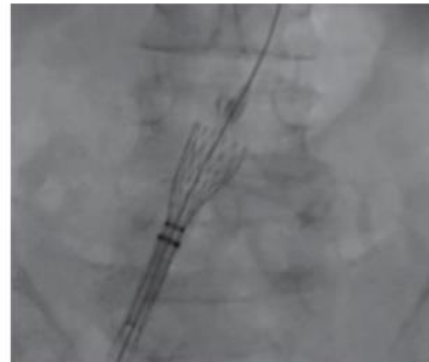
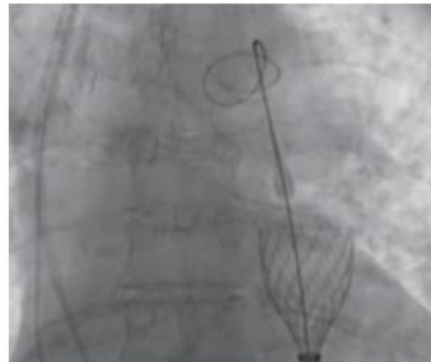
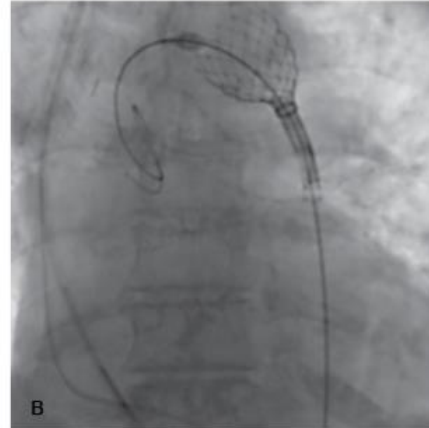
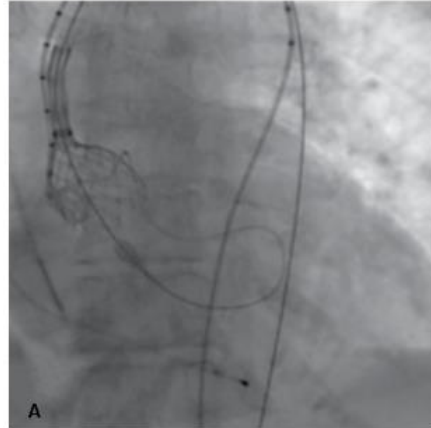
Migration of Valve into LV after deployment



Valve jumped back to descending Aorta



Gradually retrieved into working sheath



Small numbers study-27 pts

Inclusion criteria:

Normal renal function.

No previous history of stroke

EF->45%

Diabetes, Hypertension, Dyslipidemia

Only Aortic stenosis not on AR

Ages-56-90 years

Moderate to severe symptoms

Exclusion criteria

- CKD with <40 ml GFR
- EF- $<40\%$
- History of hemorrhagic stroke.
- Takayasu Arteritis.
- Severely immune compromised patients

Compared 1:1

- 14 patients were implanted TAVR under protection with pre CTA of brain and 13 patients were implanted with routine evaluation.

Primary Endpoints

- All cause mortality and stroke at 6 months and 1 year

Secondary endpoints

- Safety and acute and late stroke and neurologic deficits.

Conclusion/ Results

- CEPD significantly reduces acute and late stroke in TAVR patients at 6 months and 12 months periods.
- Devices designs and size factors also plays important role in neurological events in TAVR procedures.