

# Predictors, incidence and outcomes of patients undergoing transcatheter aortic valve implantation complicated by stroke

*From the CENTER-Collaboration*

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*On behalf of the CENTER-collaborators*



# Disclosure Statement of Financial Interest

**I, Wieneke Vlastra DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.**

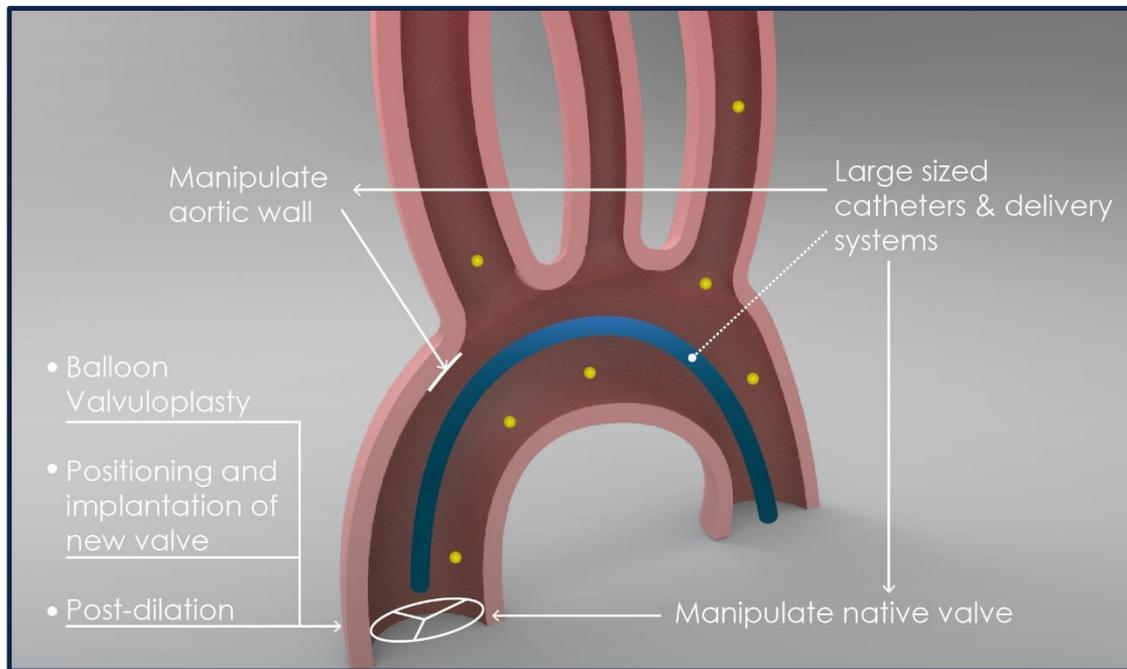
# Background

## TAVI

- **TAVI is a life-saving and minimally invasive treatment in patients with severe aortic valve stenosis**
  - The TAVI population has rapidly expanded from inoperable to intermediate-risk patients
- **Stroke remains one of the most detrimental complications of TAVI**
  - Stroke in TAVI patients increases mortality but also decreases the patient's quality of life

# Background

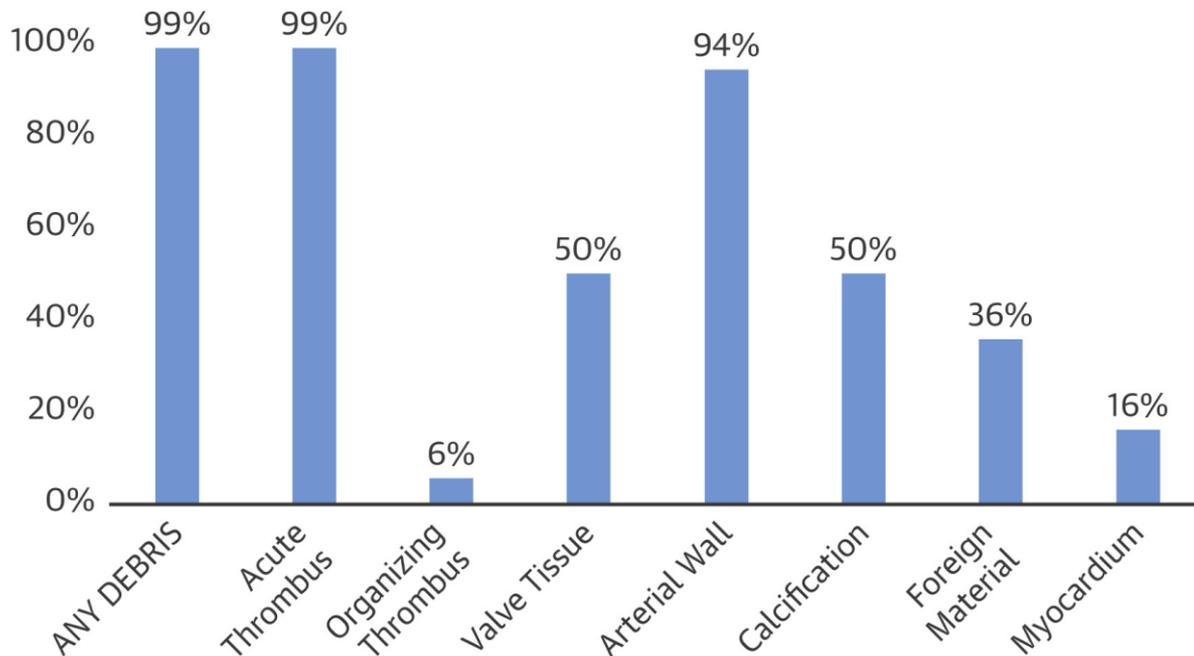
## Pathophysiology of stroke during TAVI



Vlastra et al, *J Thorac Dis* 2017

# Background

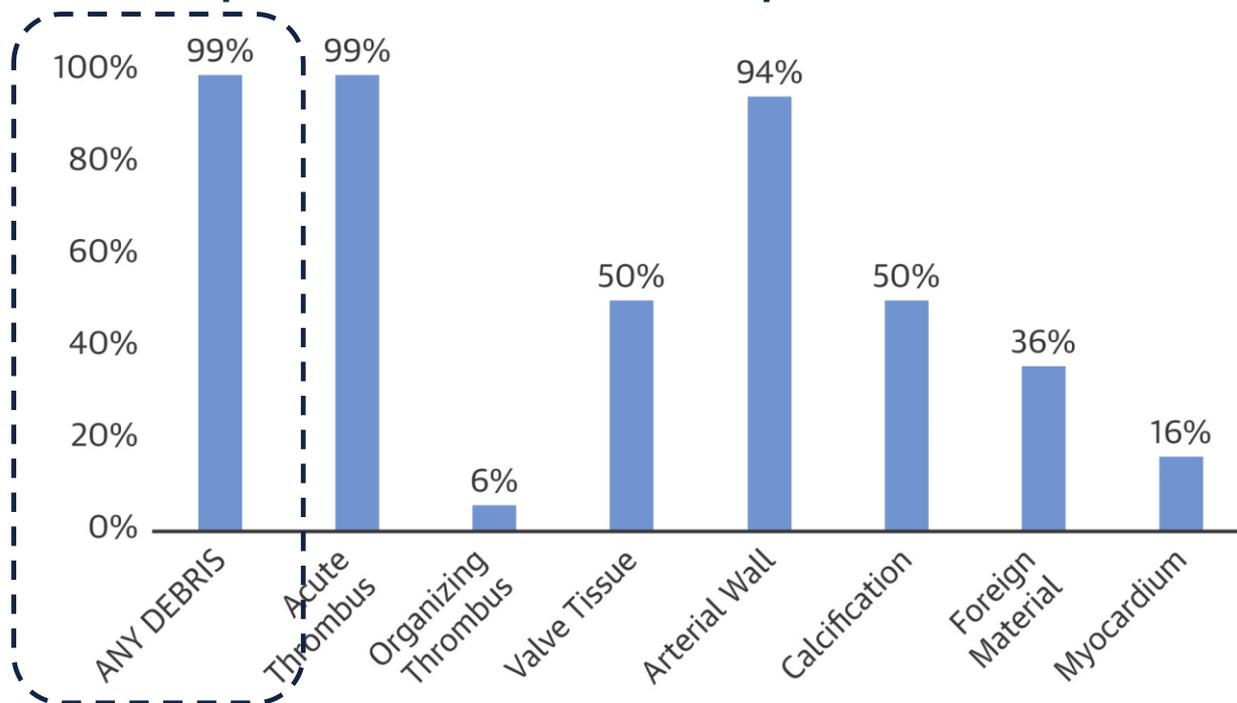
## Debris captured in cerebral protection devices



Kapadia et al, *JACC* 2017

# Background

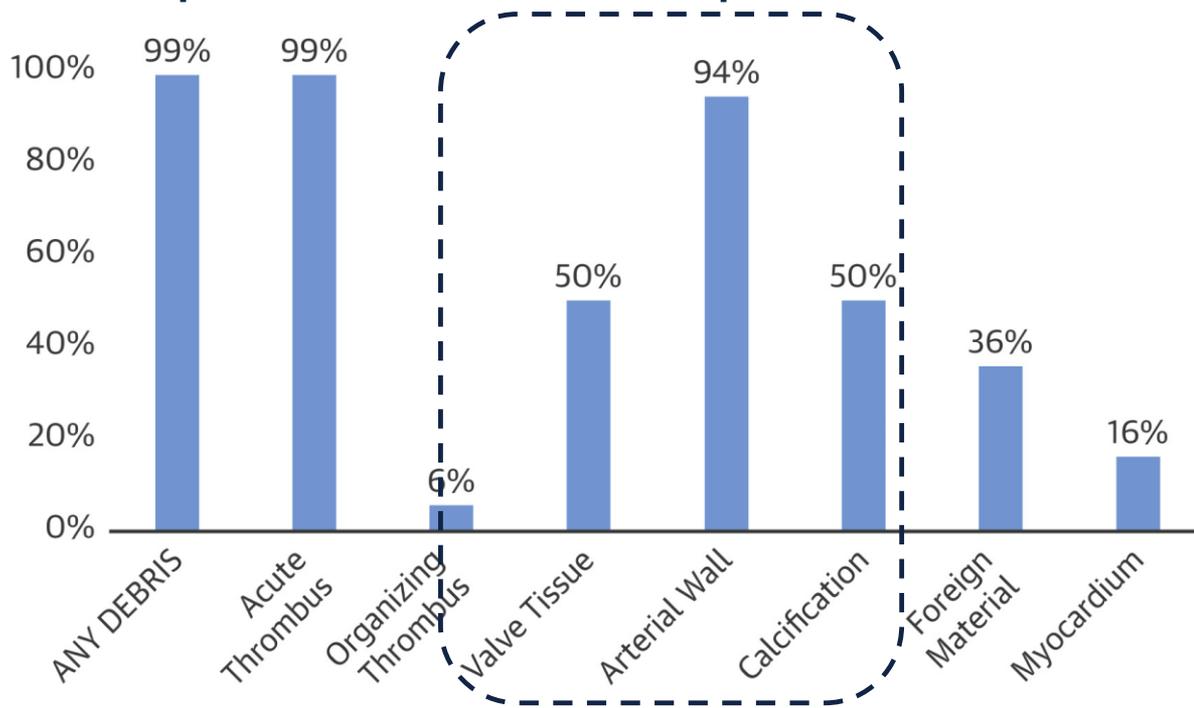
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Kapadia et al, *JACC* 2017

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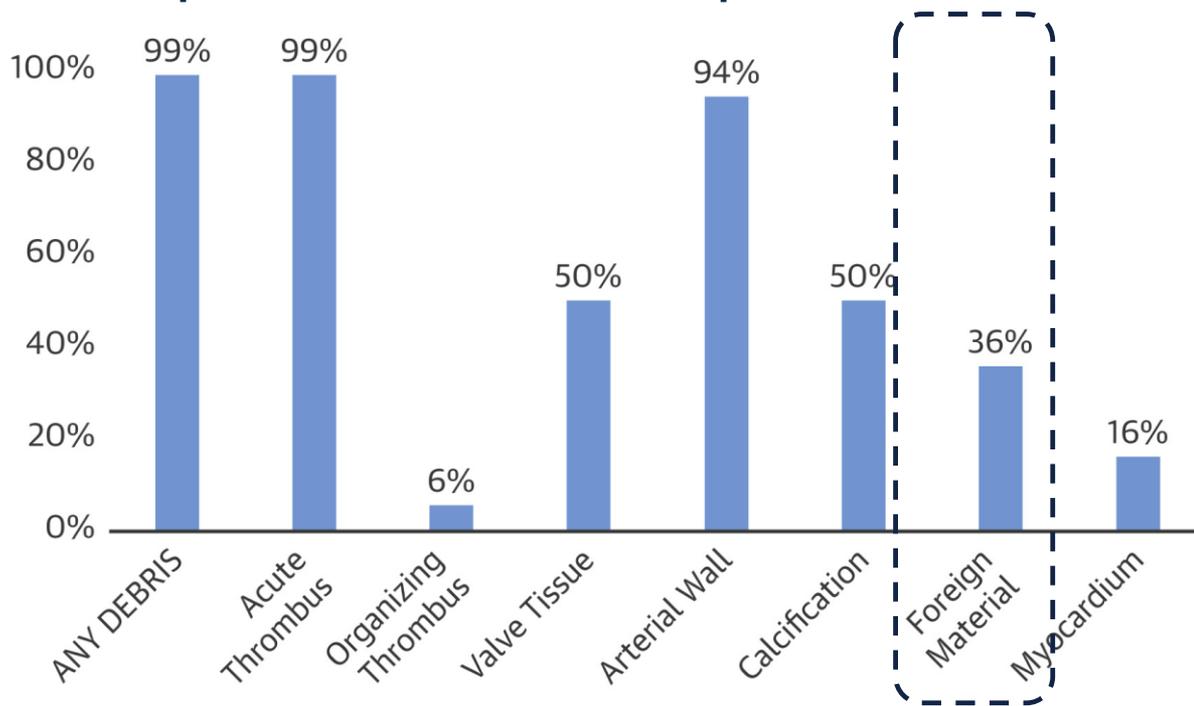
## Debris captured in cerebral protection devices



Kapadia et al, *JACC* 2017

# Background

## Debris captured in cerebral protection devices

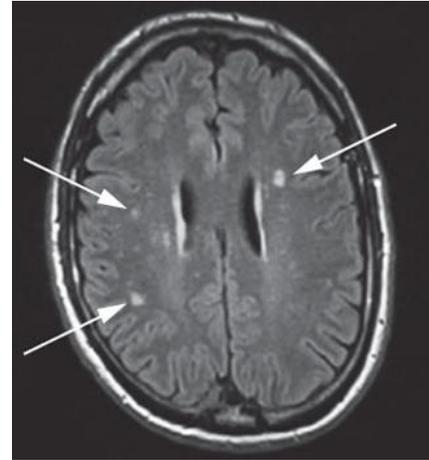


Kapadia et al, *JACC* 2017

# Background

## Cerebral infarctions after TAVI

- **Cerebral diffusion weighted magnetic resonance imaging (DW-MRI)**
  - 78% of patients (95% CI 72-83%) have new ischemic lesions after the TAVI procedure



Pagnesi et al, Int J Cardiol, 2016

Hassell et al, Nature Reviews Cardiology, 2013

# Background

## TAVI and stroke

- **Incidence of stroke**

- Reported rates vary from 1.3% to 21.0% despite development of the Valve Academic Research Consortium (VARC) criteria to promote uniformity

- **Limited data assessing patients at risk and determining clinical outcomes in patients with stroke**

- Data from large-scale, patient-level, real-world studies is needed

Généreux et al, *JACC* 2012

# Study Aim

## CENTER-Collaboration

- Determine the incidence and timeframe of 30-day stroke in TAVI patients
- Identify predictors of stroke
- Assess the impact of stroke on mortality and other clinical outcomes

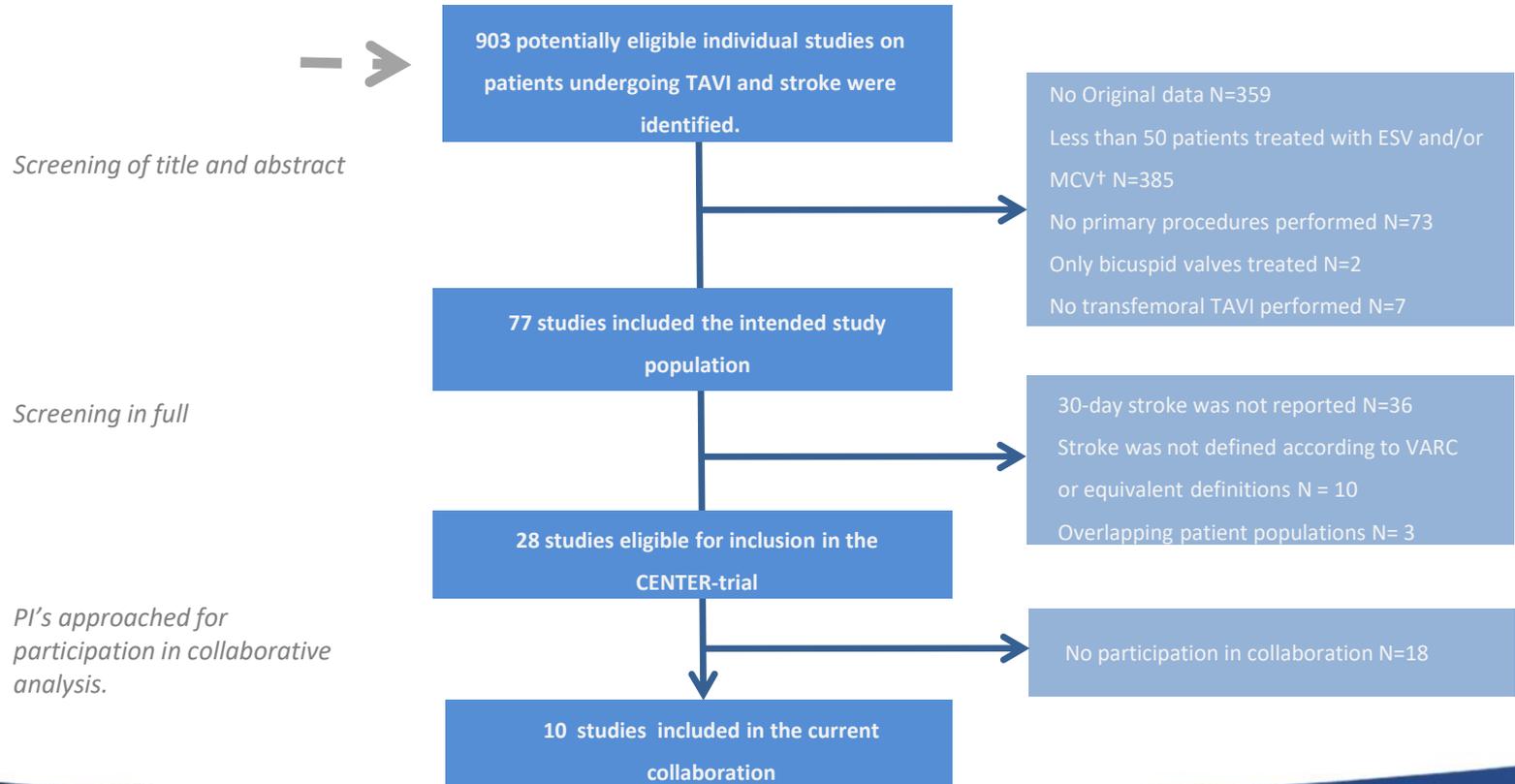
**In a large-scale, real-world & international patient population**

# CENTER-Collaboration

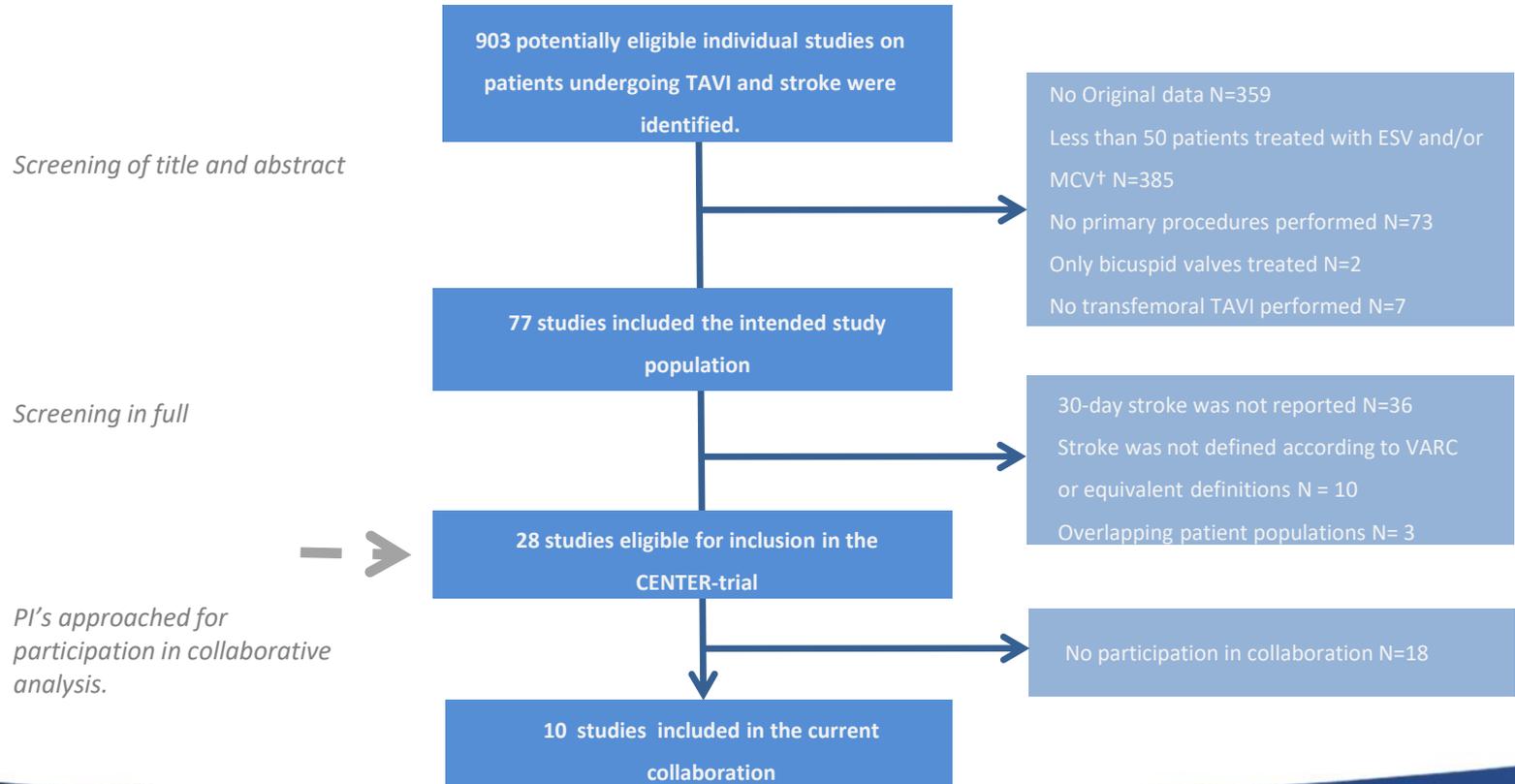
## Study selection

- Inclusion criteria for studies: including patients undergoing transfemoral TAVI with either Edwards SAPIEN valves or Medtronic CoreValves and reporting 30 day stroke outcomes

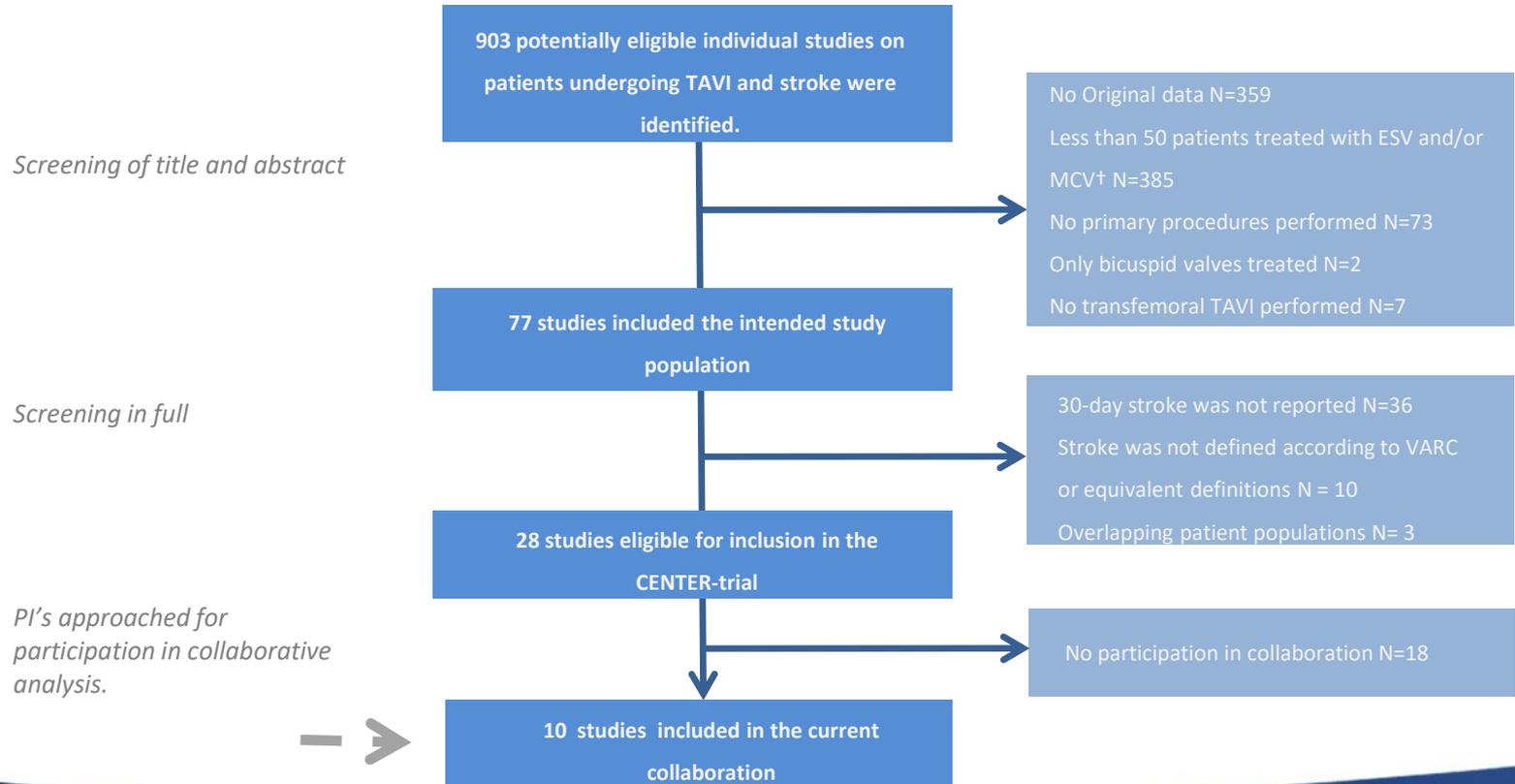
# Study selection



# Study selection



# Study selection



# CENTER-Collaboration

## Included patient populations (2007-2018)

Study	Study design	(n = 12,381)
Brazil	National registry	768
France-2	National registry	2,347
Milano	Single-centre registry	515
Verona	Single-centre registry	346
OBSERVANT	Multi-centre registry	577
Rabin	Single-centre registry (subset from multi-centre study)	544
Padova	Single-centre registry	447
Spain	National registry	5,320
BRAVO-3	Randomized controlled trial	732
WIN-TAVI	Multi-centre registry	785

# Primary and secondary endpoints

## CENTER-Collaboration

- **Primary endpoint**
  - Incidence and timeframe of 30-day stroke according to the VARC criteria
- **Secondary endpoints**
  - Predictors of stroke
  - Clinical outcomes in patients with stroke

# Baseline Patient Demographics

## CENTER-Population (N=12,381)

<b>Demographics</b>		<b>Medical history</b>	
Age (years)	81.6 ± 6.8	Previous CVA or TIA	1,246 (10%)
Female gender	7,109 (58%)	Previous ACS	1,599 (14%)
Body mass index (kg/m <sup>2</sup> )	27.1 ± 5.1	Previous PCI	1,946 (22%)
<b>Risk scores (%)</b>		Previous CABG	1,375 (12%)
Logistic EuroSCORE	14.4 (9.0-23.0)	Diabetes mellitus	3,550 (31%)
EuroSCORE II	4.0 (2.4-6.9)	Hypertension	8,603 (79%)
STS-PROM	6.4 (4.0-13.0)	Dyslipidemia	5,526 (55%)
<b>Echocardiographic characteristics</b>		Peripheral vascular disease	1,698 (15%)
Aortic max gradient (mmHg)	79 ± 23	Coronary artery disease	4,493 (43%)
Mean gradient (mmHg)	49 ± 16	Atrial fibrillation	3,029 (27%)
Aortic valve area (cm <sup>2</sup> )	0.7 ± 0.2	GFR < 30 ml/min/1.73m <sup>2</sup>	1,136 (13%)
		<b>Valve-types</b>	
		Edwards SAPIEN valve	6,239 (50%)
		Medtronic CoreValve	6,142 (50%)

# Stroke after TAVI

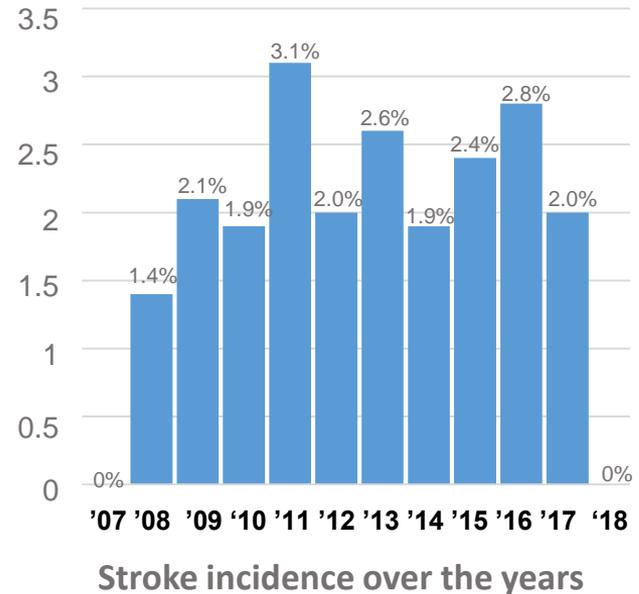
## Incidence and timeframe

- **The 30-day incidence of stroke was 2.4%**

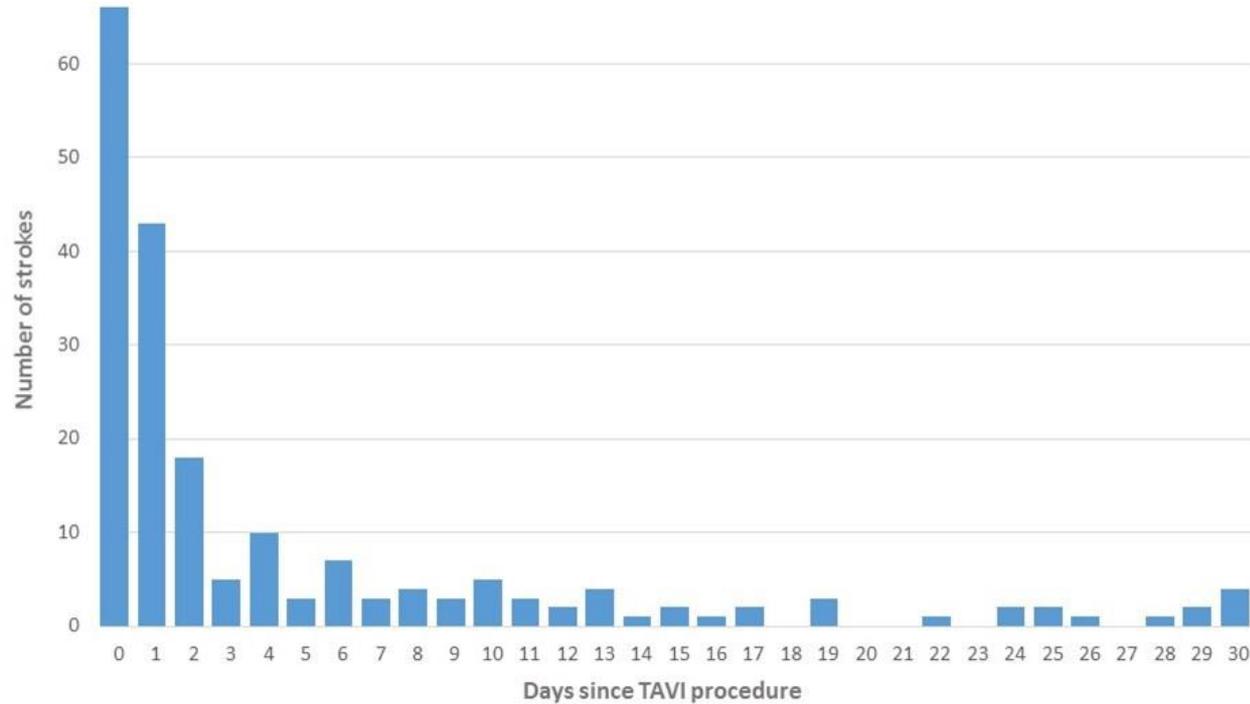
# Stroke after TAVI

## Incidence and timeframe

- The 30-day incidence of stroke was **2.4%**
- The incidence of stroke was equal in the early years and late years of TAVI ( $p = 1.0$ )
  - 2007-2012: 2.4%
  - 2013-2018: 2.4%

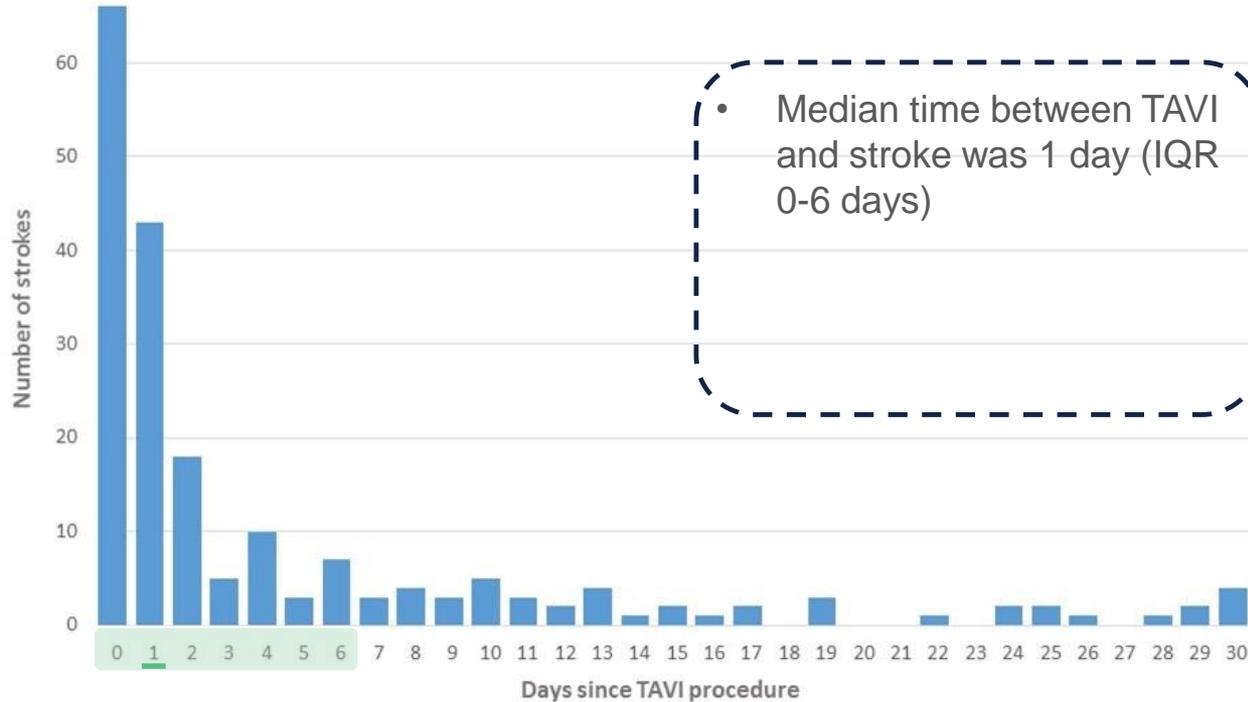


# Timing of Stroke after TAVI



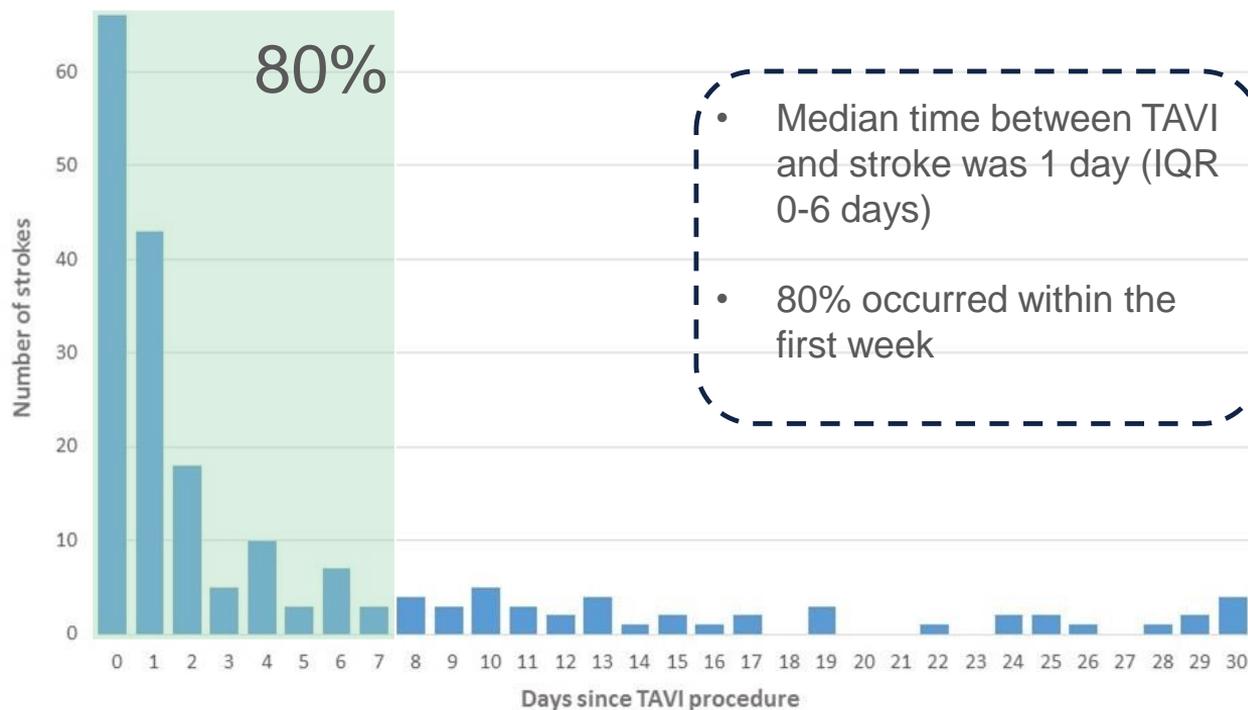
# Study Aim

## Timing of stroke after TAVI



# Study Aim

## Timing of stroke after TAVI



# Cerebrovascular events after TAVI

- **Stroke was defined as major stroke in 75%**
- **The incidence of TIA at 30 days was 0.6%**
- **The cumulative stroke rate increased from 2.4% at 30 days to 5% at 1 year**

# Stroke after TAVI

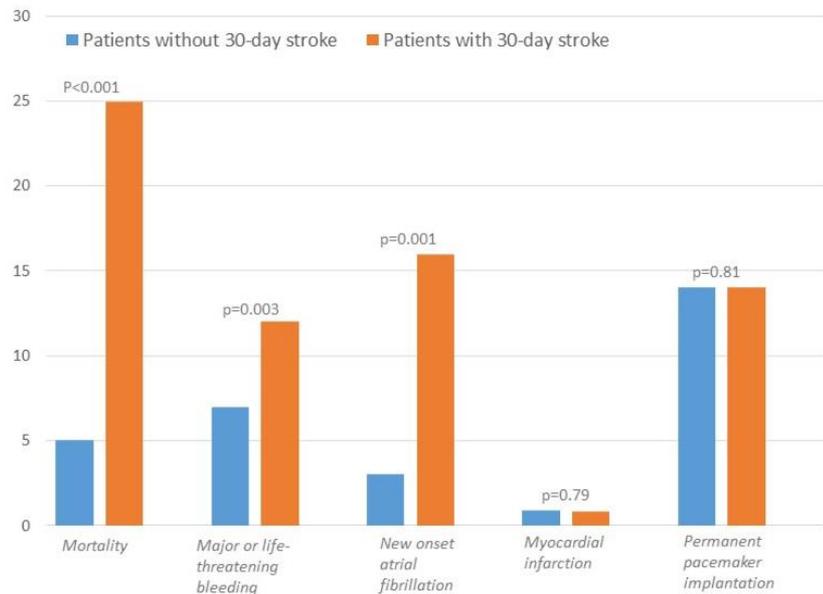
## Predictors

- **Predictors of 30-day stroke in multivariate regression analysis**
  - Previous cerebrovascular events OR 2.1 (95%CI 1.4-3.3) p=0.001
  - GFR of less than 30 ml/min/1.73m<sup>2</sup> OR 1.6 (95% CI 1.0-2.5) p=0.03

	No stroke at 30 days (n = 10,721)	Stroke at 30 days (n = 261)	p-value
Previous CVA or TIA	1057 (10%)	43 (17%)	<0.001
GFR < 30 ml/min/1.73m <sup>2</sup>	1013 (13%)	33 (19%)	0.03

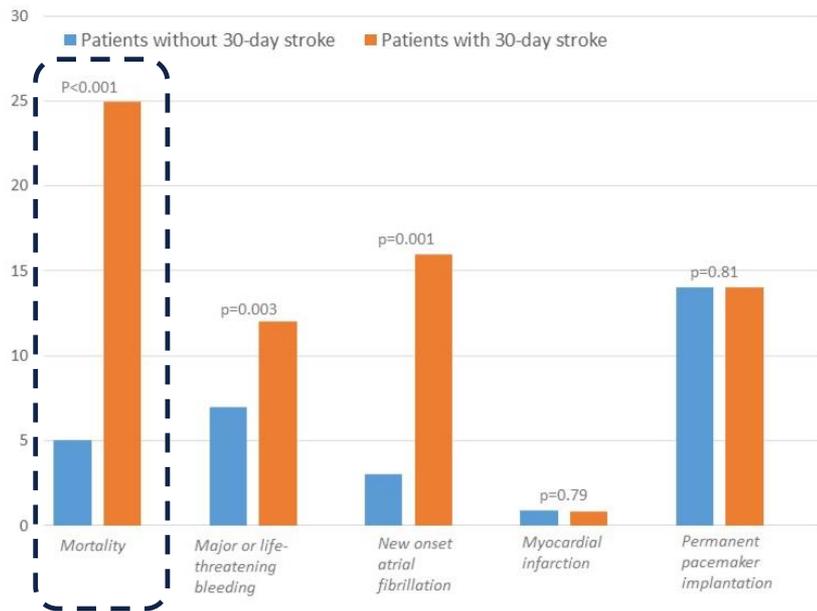
# 30-day clinical outcomes (%)

## In patients with and without stroke



# 30-day clinical outcomes (%)

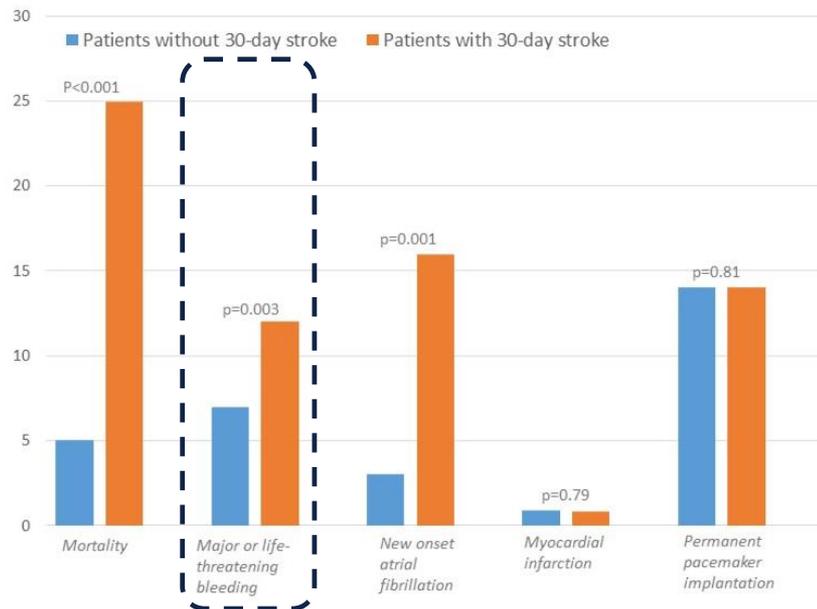
## In patients with and without stroke



- **Six-fold increase in mortality**  
OR 6.0, 95% CI 4.4-8.1,  $p < 0.001$

# 30-day clinical outcomes (%)

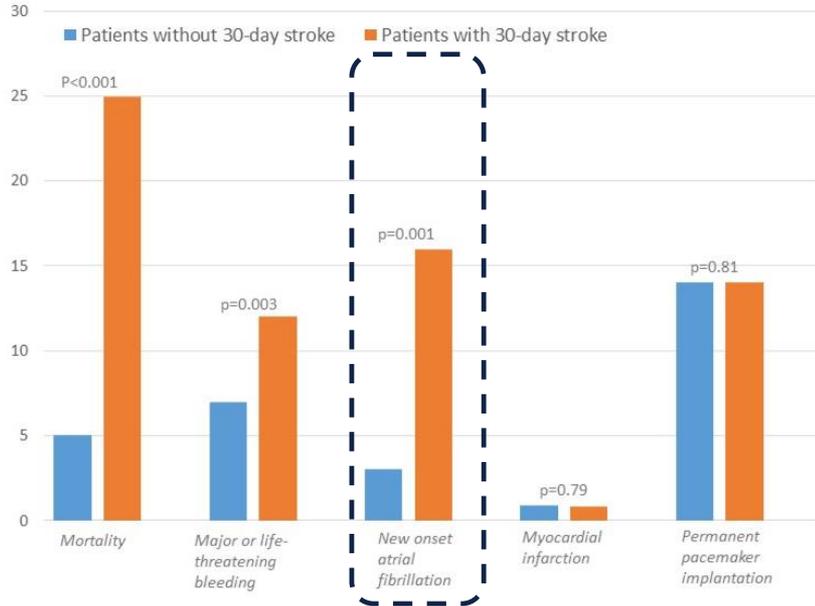
## In patients with and without stroke



- **Six-fold increase in mortality**  
OR 6.0, 95% CI 4.4-8.1,  $p < 0.001$
- **Two-fold increase in major or life-threatening bleeding**  
OR 1.9, 95% CI 1.3-3.0,  $p = 0.003$

# 30-day clinical outcomes (%)

## In patients with and without stroke



- **Six-fold increase in mortality**  
OR 6.0, 95% CI 4.4-8.1,  $p < 0.001$
- **Two-fold increase in major or life-threatening bleeding**  
OR 1.9, 95% CI 1.3-3.0,  $p = 0.003$
- **Five-fold more frequent new-onset atrial fibrillation**  
OR 5.2, 95% CI 1.9-14.1,  $p = 0.001$

# Conclusions

## CENTER-Collaboration

- The 30-day incidence of stroke after TAVI was 2.4%, this was consistent over time
- 80% of the strokes occurred during the first week after TAVI
- Patients with prior cerebrovascular events or a low GFR were at higher risk for stroke
- There was a strong association between new-onset atrial fibrillation and stroke
- Stroke was associated with a six-fold increase of 30-day mortality and a two-fold higher risk of major or life-threatening bleedings

# Discussion

## CENTER-Collaboration

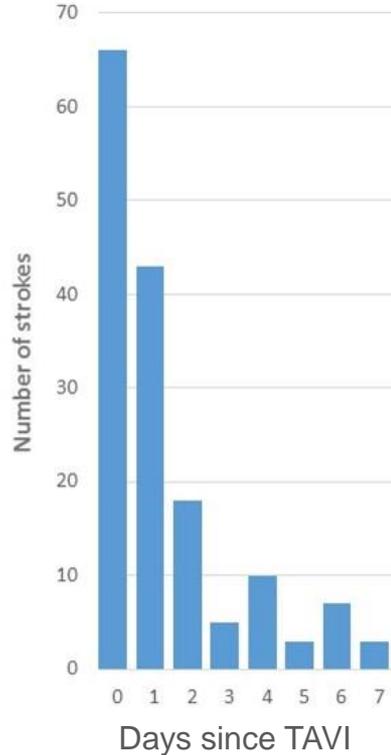
- **Study design**
  - Heterogeneous studies
  - Not all studies had independent adjudication of clinical events
  - Newest valve types were used in a minimum amount of patients

# Discussion

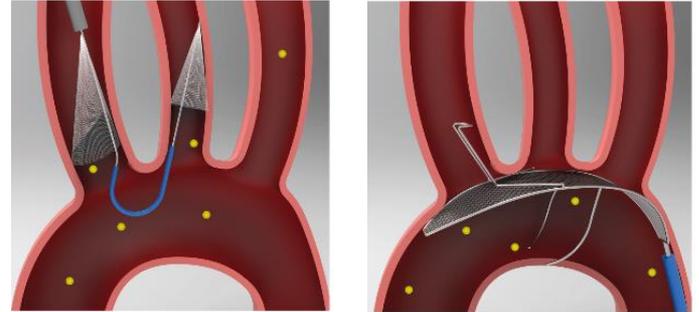
## CENTER-Collaboration

- **Study design**
  - Heterogeneous studies
  - Not all studies had independent adjudication of clinical events
  - Newest valve types were used in a minimum amount of patients
- **Reflection of current practice of TAVI during the past decade (across the globe)**

# Need to reduce stroke



- **Incidence over time – poor outcomes**
- **The majority of strokes are directly post-procedure**
  - Patient/device selection (?)
  - Cerebral protection devices (?)
  - NOAC (?)



# CENTER-trial Collaborators

- **Spanish TAVI registry**
  - Pilar Jimenez-Quevedo
  - Jose M de la Torre
  - Rosana Hernandez-Antolin
- **FRANCE-2**
  - Didier Tchétché
  - Nicolas Dumonteil
  - Thomas Modine
- **BRAVO-3 & WIN-TAVI**
  - Jaya Chandrasekhar
  - Samantha Sartori
  - Roxana Mehran
- **National Brazilian TAVI registry**
  - Fabio S. de Brito
  - Rogério Sarmento-Leite
- **OBSERVANT**
  - Marco Barbanti
  - Paola D'Errigo
- **Rabin medical centre**
  - Ran Kornowski
  - Katia Orvin
- **Milano**
  - Azeem Latib
  - Matteo Pagnesi
- **Padova**
  - Augusto D'Onofrio
  - Chiara Fraccaro
- **Verona**
  - Flavio Ribichini
  - Mattia Lunardi
- **Amsterdam UMC**
  - Jan Baan
  - Jan Tijssen
  - Jan Piek
  - Ronak Delewi

# Conclusions

## CENTER-Collaboration

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